LIVER FUNCTION TESTS IN CONGESTIVE CARDIAC FAILURE

DISSERTATION SUBMITTED TO

THE TAMIL NADU DR.M.G.R MEDICAL UNIVERSITY

IN PARTIAL FULFILLMENT OF THE REGULATIONS

FOR THE AWARD OF THE DEGREE OF

M.D (GENERAL MEDICINE) BRANCH – I

TIRUNELVELI GOVT. MEDICAL COLLEGE & HOSPITAL

TIRUNELVELI

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

CHENNAI, TAMIL NADU

APRIL 2013

CERTIFICATE

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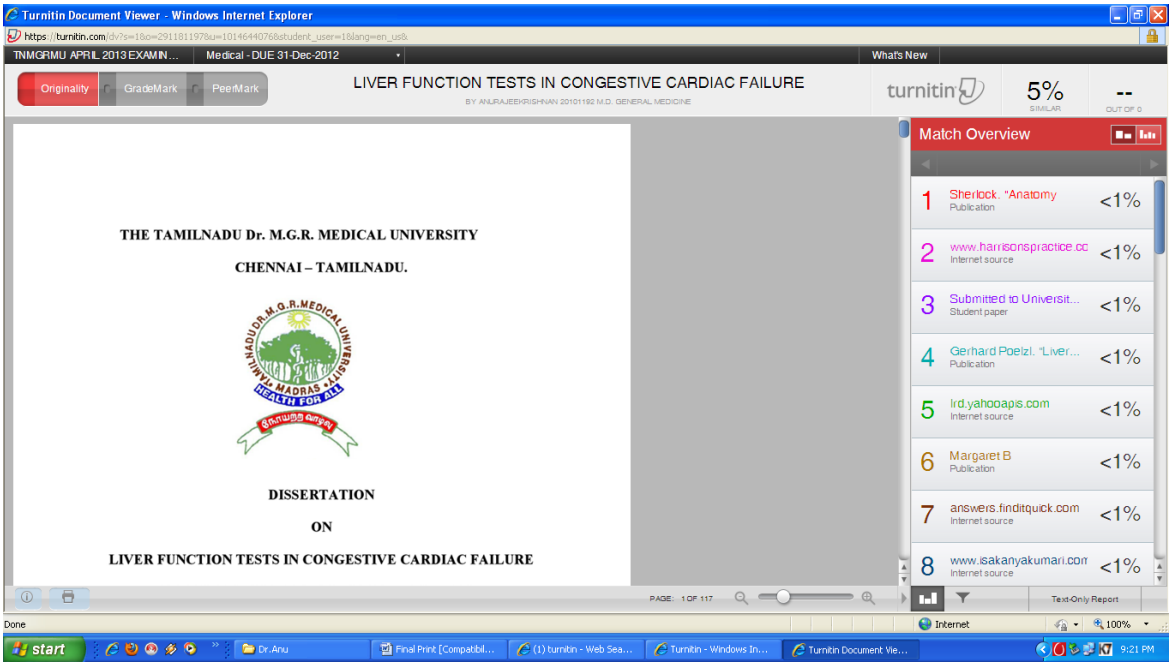
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I solemnly declare that the dissertation titled " **LIVER FUNCTION TESTS IN CONGESTIVE CARDIAC FAILURE''** was done by me at Tirunelveli Government Medical College and Hospital during 2011-2012 under the guidance and supervision of **PROF. DR.S.S.NAZAR M.D.,**Professor of Medicine.

This dissertation is submitted to the **Tamil Nadu Dr.M.G.R Medical University** towards the partial fulfillment of requirements for the award of **M.D DEGREE (BRANCH-I)** in General Medicine.

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ACKNOWLEDGEMENT

I am extremely grateful to **The DEAN, DR.MANOHARAN M.S,** Tirunelveli Medical College for granting me permission to do this dissertation work in Tirunelveli Medical college Hospital, Tirunelveli.

I express my sincere gratitude to the professor and the Head of the Department of medicine **Prof. Dr.R.GEETHARANI, M.D.,** for her valuable support and guidance in preparing this dissertation.

I am greatly indebted to my unit chief and beloved teacher **Prof.Dr.S.S.NAZAR M D,** who inspired, encouraged and guided me in every step of this study.

I am grateful to Professor **Dr.RAVICHANDRAN EDWIN, M.D, D.M,** Professor and Head of Department of Cardiology,Tirunelveli Medical College for his guidance in doing this study.

I am grateful to **Dr.BALACHANDRAN, M.D, D.M,** Assistant Professor of

Cardiology, **Dr.KANDASAMY PRABHU, M.D,D.M,** Assistant Professor of Gastroenterology, for their guidance and support throughout the study.

I am thankful to beloved Assistant Professors of my unit, **Dr.RAJESH BABU, M.D. and Dr. SHAVANA, M.D.,** for their guidance and help throughout this work.

I thank the Department of Biochemistry for their help in investigation aspects.

I express my gratitude to all the patients who participated in this study without whom this study would not have been possible.

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LIST OF ABBREVATIONS

1.	LFT	Liver function tests
2.	CCF	Congestive cardiac failure
3.	CAHD	Coronary artery heart disease
4.	CP	Cor pulmonale
5.	RHD	Rheumatic heart disease
6.	CM	Cardiomyopathy
7.	HHD	Hypertensive heart disease
8.	AST/SGOT	Aspartate amnotransferase/Serum glutamic oxaloacetic transaminase
9.	ALT/SGPT	Alanine aminotransferase/Serum glutamic pyruvate transaminase
10.	ALP	Alkaline phosphatase
11.	GGT	Gamma glutamyl transpeptidase.
12.	ECG	Electrocardiogram
13.	CLN	Centrilobular necrosis

INTRODUCTION

Liver is the biggest organ in human body with a mass of nearly 1.5 kg[2]. Liver has a massive functional reserve and regenerating capacity. It plays a major role in maintaining the normal physiology and metabolic homeostasis of human body. It is also referred to as the custodian of milieu interior[7]. Hence hepatic diseases can have a major impact on the homeostasis of body. Similarly disorders in other systems can adversely affect the liver as well.

Cardiac failure both chronic and acute can cause hepatic dysfunction [1]. Twenty five percent of total cardiac output goes to the liver,hence any decrease in cardiac output leads to decreased liver perfusion.by means of vasoregulatory mechanisms and enhanced extraction of oxygen liver can tolerate variations in blood flow.

But hepatic damage occurs when the threshold levels are crossed.In right heart decompensation raised backpressure causes congestion of the sinusoids and hepatocyte hypoxia. Left heart failure produces decreased cardiac output further causing decreased blood flow to the liver producing hypoxia. Both this mechanisms leads eventually into centrilobular liver cell necrosis. The most susceptible region of the liver lobule to hypoxic insult is the zone three of acini because of the peculiar arrangement of blood flow in the liver.

In the present study ,the consequence of congestive cardiac failure on liver function were studied in a group of 60 patients and was analysed and compared with various parameters.Differing causes of heart failure of various duration were included in the study. Follow up of the cases were done for a period of one week and measurements were repeated at the end of one week. Changes in the values were recorded and an attempt is done to find the prevalence of liver function abnormalities in these subjects,its correlation with various parameters and prognostic significance of liver function on cardiac failure.

A proper knowledge and understanding of structure and functions of liver,liver parameters,etiologies and different forms of heart failure and their presentation ,as well as the mechanism and pathology of liver in cardiac failure is inevitable before assessing the liver function abnormalities in congestive cardiac failure.

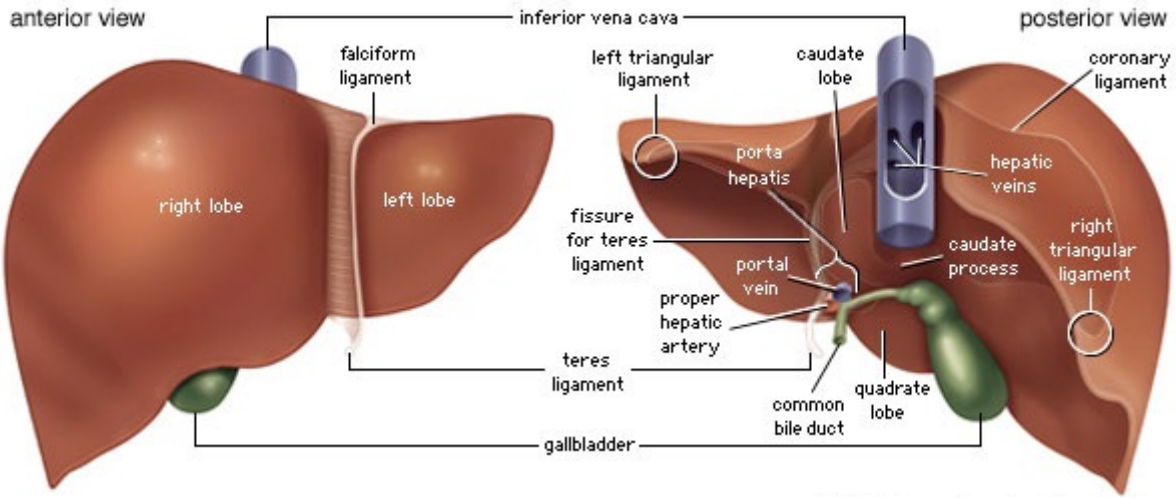
AIMS AND OBJECTIVES

1. To study the prevalence of liver function abnormalities in congestive cardiac failure patients attending Tirunelveli Medical College Hospital
2. To assess the correlation of liver function tests with etiology , duration and NYHA Class of cardiac failure
3. To study the pattern of elevation of liver enzymes in cardiac failure.
4. To study the prognostic importance of liver function abnormalities in cardiac failure

REVIEW OF LITERATURE

STRUCTURE AND FUNCTIONS OF LIVER

The liver weighing 1.2–1.5kg forms one-fiftieth of the whole body mass and is the biggest structure in human being[2]. Liver is situated in the right upper abdomen .It extends from the fifth ICS in the MCL to right rib boundary. During inspiration the lower margin of the liver crosses the rib border. Other surfaces of liver fit alongside the diaphragm and are even and rounded . Right kidney, colon and duodenum form markings on the posterior surface of right lobe of liver and on left lobe stomach[3]. Peritoneal reflections like the right and left triangular ligaments ,coronary ligaments and the falciform ligament hold the liver in position. The liver is connected to the upper portion of duodenum by the hepatoduodenal ligament. The portal vein, hepatic artery, bile duct, lymphatic vessels and nerves are present in the free border of this ligament. The falciform ligament divides the liver into left and right lobes[2] .The liver is classified into eight segments, supplied by hepatic and portal branches and bileductules and hepatic venules present among the segments[3].


anterior view
posterior view
inferior vena cava
falciform ligament
left triangular ligament
caudate lobe
coronary ligament
porta hepatis
hepatic veins
right lobe
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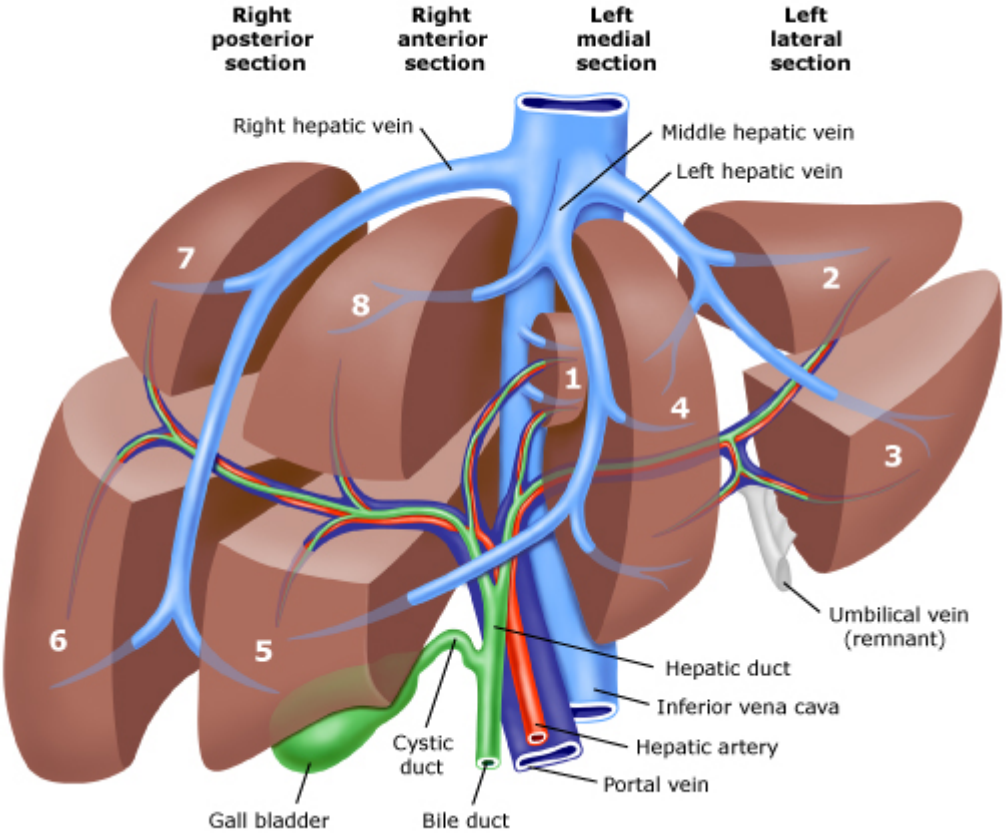
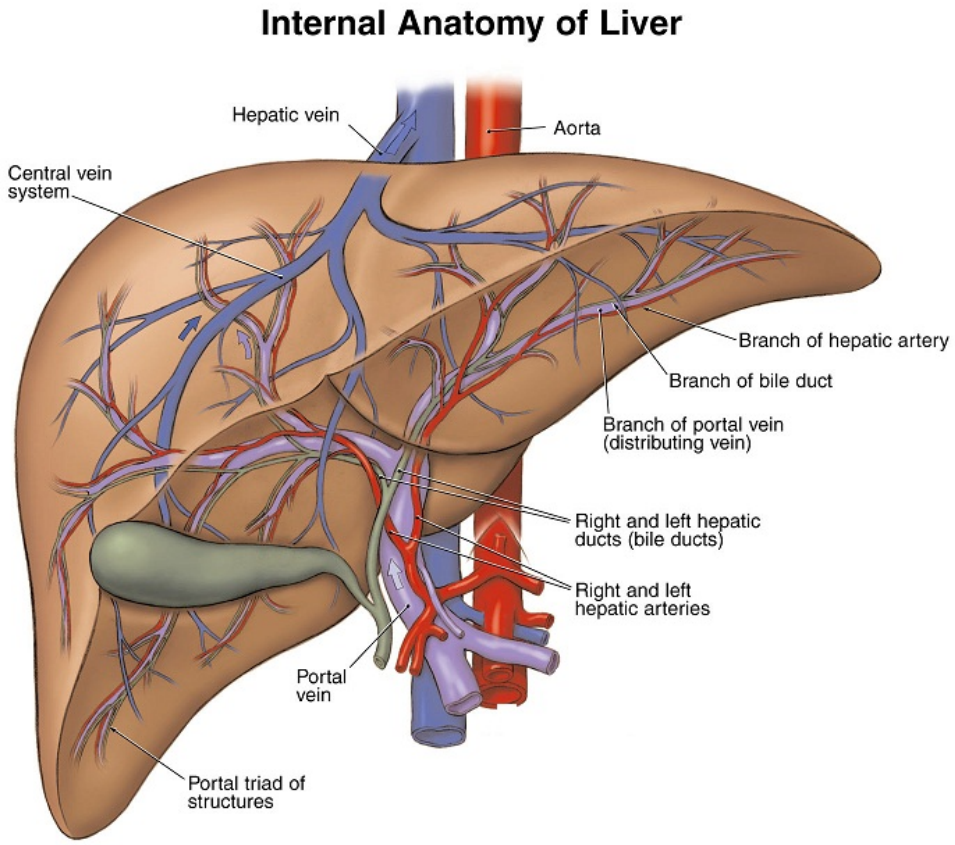
teres ligament
common bile duct
quadrate lobe
gallbladder


Right posterior section
Right anterior section
Left medial section
Left lateral section
Right hepatic vein
Middle hepatic vein
Left hepatic vein
7
8
2
1
4
3
6
5
Umbilical vein (remnant)
Hepatic duct
Inferior vena cava
Cystic duct
Hepatic artery
Portal vein
Gall bladder
Bile duct

Blood circulation to the hepatic tissue has peculiar features.It has both systemic and portal circulation[3].Arterial blood is supplied bythe hepatic artery, originating from the coeliac axis .The portal circulation consists of venous blood from spleen, intestines etc. The porta hepatis fissure, which lies on undersurface of the right lobe is the portal of entry for this vessels[9]. On entry into liver hepatic artery and portal vein divide into right and left lobe branches. Common bile duct is formed by confluence of right and left hepatic ducts in the porta. Sympathetic fibres from ganglia T7–T10 supplies the liver through the hepatic plexus[1].

The CBD(common bile duct) is situated in front and right side of hepatic artery and in front of portalvein. Within the portal tracts intrahepatic bile ducts strictly track the path of intrahepatic arteries and portal veins. Right and left hepatic veins drain venous blood from the liver. They arise from posterior aspect of liver and drain into IVC(inferior vena cava) close to its entry point to right atrium. Collection of lymph nodes nearby portahepatis and coeliac axis drain the lymph. The mediastinal glands receives superficial hepatic lymph vessels traverse the diaphragm .One more group drains in some minor glands nearby IVC intrathoracic part[2.3].

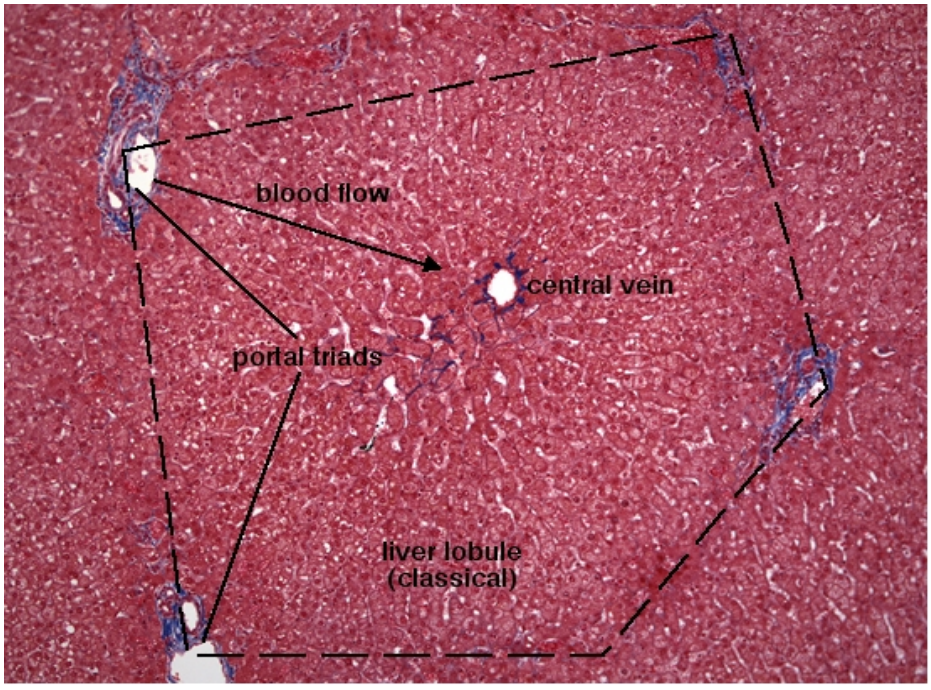


Except in three places the liver is entirely enclosed within peritoneum. There is a bare area near the IVC fossa where liver is in straight contact with the diaphragm. IVC fossa and gallbladder fossa lacks peritoneal covering[1]. The peritoneal ligament and the intra-abdominal pressure keep the liver in position.

FUNCTIONAL ANATOMY

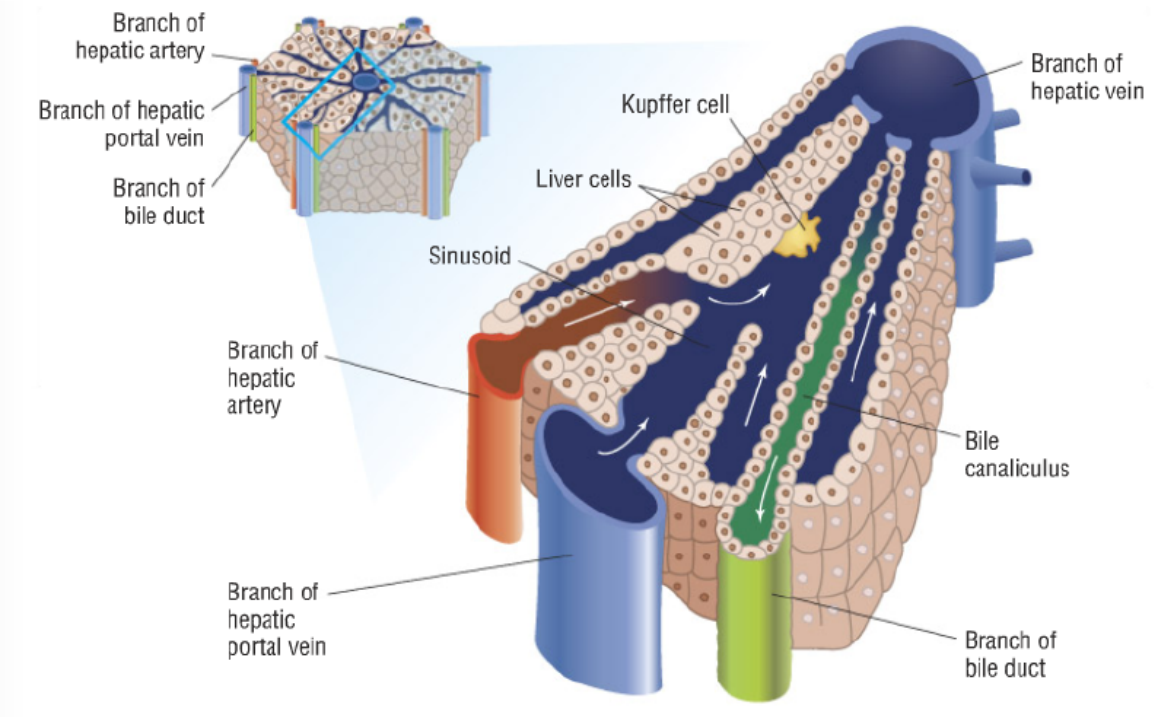
The model of hepatic lobular architecture was put forward by Kierman et al[29] in 1833.Thepyramidal lobules comprises of a peripheral portal tract made up of portal vein radicle, hepatic artery branch and the bile duct and a central tract of the hepatic vein[3]. Blood-containing sinusoids and

columns of hepatocytes spread between above two structures. The hepatic vein radicles and their adventitia occupy the central hepatic canals. They are enclosed by hepatocytes. The hepatic arteriole, the portal vein radicle and bile duct along with a few number of cells and connective tissue form the portal triad. The major portion of liver about 60% is made up of hepatocytes[3,9] .They are nearly 30mm in diameter and multilateral. The liver cells has three surfaces: each fronting the canaliculus, the sinusoid and space of Disse, neighbouring hepatocytes respectively. The lifetime of hepatocytes nearly 150 days. They lack basement membrane[2].



Endothelial cells line the sinusoids. The sinusoids contain the Kupffer cells(phagocytic cells of thereticulo-endothelial system), the fat storing cells(hepatic stellate cells, Ito cells or lipocytes), liver cells and sinusoidal

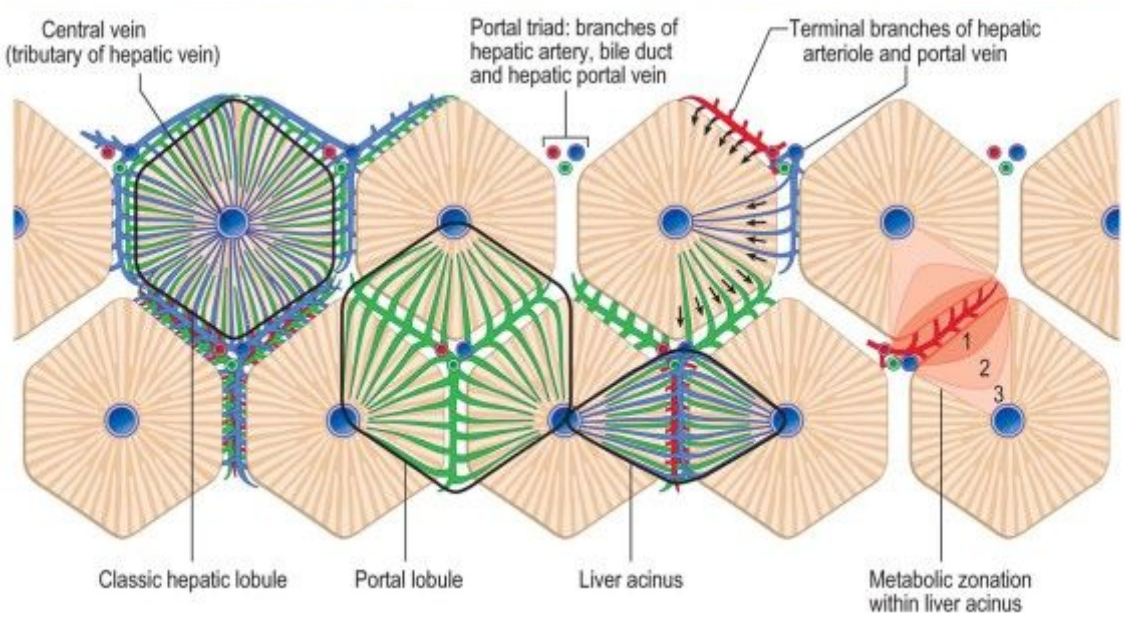
endothelial cells. Space of Disse is a tissue space between liver cells and endothelium of sinusoids. Connective tissue around the portal region contains liver lymphatics which has an endothelial lining. Lymphatics receive lymph through the endothelium. The division of the hepatic artery delivers blood to the contents in portal tracts forming a network surrounding biliary ductules .These arterioles drains into sinusoids at multiple points .Portal veins and hepatic arterioles do not anastamose directly[2].



Bile canaliculi are the main portals of elimination of liver. They are channels between the apposition surfaces of hepatocytes with no separate lining. The cytoskeleton of liver cells is made up of microfilaments supporting the cell membrane .Microvilli are found on the exterior of cells[12]. Canals of Hering are thin-walled terminal bile ducts or ductules lined with cuboidal epithelium that drain the intralobular canaliculi which eventually

end in bile ducts in the portal canals Desmosomes, tight junctions and gap junctions separate canaliculi from other cell surface.

Functionally liver is structured into acini, with hepatic arterial and portal venous blood entering the acinus from the portal areas which constitute zone1 and flows through the sinusoids to the terminal hepatic veins zone3[9] . The intervening liver cells constitute zone2. Hence zone3 of liver is susceptible to toxic and anoxic insult. Bile flows in the reverse direction from zone3 to zone1. The cells in the border of acini , zone3 differ in function from those of cells in zone 1. TCA cycle enzymes are more in periportal zone . Glutamic synthetase is present in zone 3. Perivenous zone is susceptible to anoxic injury. Congestive heart failure disturbs zone 3 of the hepatic acini leading to distinctive features [9].



LIVER FUNCTIONS

Liver cells execute many essential roles in maintaining homeostasis and well-being.

SYNTHETIC FUNCTIONS

The synthesis of proteins like carrier proteins, albumin, hormones, growth factors, coagulation factors, bile and transporters like bileacids, cholesterol, lecithin, phospholipids[1].

DIGESTIVE FUNCTIONS

Nutrients like glucose, glycogen, lipids, cholesterol, amino acids stored and metabolized by liver[1,2]. Liver also carries out metabolism and conjugation of lipophilic compounds (bilirubin, anions, cations, drugs)

EXCRETORY FUNCTIONS

This include metabolism of hormones including insulin and others Bilirubin undergo conjugation in the liver to form mono and di glucoronides which is eliminated through bile. The liver metabolises and detoxify toxic substances through reactions like methylation. It also act upon drug products and detoxify them through a process referred to as drug metabolism. The drugs and toxic products are thus metabolized and conjugated and eliminated in urine or bile[1,3] .The site of Urea cycle where conversion of ammonia to urea occurs is in the liver.

STORAGE

Storage of an array of various substances occur in the liver which includes glucose as glycogen, vitamin B12, vitamin A, vitamin K, vitamin D, copper and iron.

IMMUNE FUNCTIONS

The liver plays a major role in immunological reactions. In the liver RES (reticuloendothelial system) is constituted mainly by cells that are immunologically reactive. Liver acts as a 'sieve' for antigens reaching it through the portal circulation[1].

LIVER FUNCTION TESTS

The evaluation and management of patients with hepatic dysfunction is done by means of a variety of liver function tests. The tests are used to (1) distinguish the presence and absence of liver illness, (2) differentiate among a variety of liver disorders, (3) estimate the amount of hepatic damage, and (4) monitor the outcome following treatment[48]. The constellation of laboratory tests that involve hepatic synthetic function (serum albumin and prothrombin time), liver enzymes, and the serum bilirubin level is referred to as liver biochemical tests or liver function tests .The serum albumin and prothrombin time measures protein synthesis, serum bilirubin measures hepatic conjugation and excretion. Liver dysfunction is characterized by abnormalities of bilirubin ,albumin and prothrombin time. Liver failure is incompatible with life and hepatic functions are intricate and varied to be

substituted by a mechanical pump ; dialysis membrane or fabrication of instilled proteins, growth factors and proteins[1].

Tests Centered on Conjugation and Elimination Purposes

SERUM BILIRUBIN

Bilirubin, a yellow breakdown product of heme catabolism and is present in blood in two forms—conjugated and unconjugated. The unconjugated form or the indirect fraction, does not dissolve in water and is carried by albumin in the circulation. The conjugated or direct bilirubin fraction dissolves in water and is eliminated by renal system. Estimated by the van den Bergh method, the total serum bilirubin concentration is normally<17mol/L (1 mg/dL).Of these 30%, or 5.1mol/L (0.3 mg/dL) is constituted by direct-reacting bilirubin [48].

Rise of the indirect fraction of bilirubin is hardly due to hepatic dysfunction. Isolated increase of indirect bilirubin is found predominantly in hemolytic conditions and genetic disorders like Crigler-Najjar and Gilbert's syndromes. Isolated indirect hyperbilirubinemia (bilirubin increased but <15% conjugated) must warrant adiagnosis of hemolysis . An isolated indirect hyperbilirubinemia without hemolysis can be ascribed to Gilbert's syndrome and no additional assessment is needed.

Isolated direct hyperbilirubinemia usually indicates hepatic or biliary tract disease. The passage of direct bilirubin into the biliary canaliculi is the rate limiting step in bilirubin breakdown. Hence increase in the conjugated

form can be seen in almost any kind of hepatic disorder. Both direct and indirect forms of the bilirubin is likely to be elevated in most of liver disease.

SERUM ENZYMES

The liver comprises of numerous enzymes, of which some are found in the serum in small concentrations. These enzymes act like other serum proteins with no known function . These enzymes are dispersed in the interstitial fluid ,plasma and have distinctive half-lives, typically estimated in days. Enzymes are possibly cleared by cells in the reticuloendothelial system. The increase in particular enzyme action in the serum is assumed to chiefly mirror its increased rate of entry into serum from injured hepatocytes Serum enzyme tests can be assembled into three classes: (1) enzymes whose rise in serum mirrors injury to hepatic cells, (2) enzymes whose rise in serum mirrors cholestasis, and (3) enzyme tests with no specific pattern.

Enzymes that indicates destruction to Hepatocytes

The transaminases (aminotransferases) are reliable pointers of liver cell injury. These tests are of great use in differentiating liver ailments like hepatitis. They include the aspartate aminotransferase (AST or SGOT) and the alanine aminotransferase (ALT or SGPT). SGOT is identified in tissues including liver cells, cardiac muscle, skeletal muscle, kidneys, brain, pancreas, lungs, WBC and RBC in descending order of concentration. SGPT is present chiefly in the hepatocytes. The aminotransferases are routinely found in serum in small amounts. They are delivered into the

circulation in larger amounts when there is injury to the hepatocyte membrane leading to easy permeability. Hepatocyte necrosis is not needed for the discharge of the aminotransferases, and the correlation between the amount of hepatocyte damage and the level of the aminotransferases is poor. Hence, the outright increase in aminotransferase has nil prognostic implication in acute hepatocellular conditions. Any kind of liver cell damage can produce a modest rise in the serum aminotransferases.Values of up to 300 U/L can be present in any kind of hepatic disorder and are nonspecific[49] . Studies have revealed that fatty liver disease is the most likely explanation for mild ALT elevations in asymptomatic blood donors[50].

Remarkable rises with aminotransferases > 1000 U/L is seen almost absolutely in conditions linked with widespread hepatocellular damage such as[31]

1. hepatic damage due to ischaemia
2. hepatic injury secondary to toxins and medications
3. (3)hepatitis due to viral infections.

The estimation of transaminase increase can be of great use in diagnosis. Usually ALT is greater than or equivalent to the AST in acute liver cell conditions. An AST:ALTproportion > 2:1 is indicative whereas a proportion> 3:1 is greatly indicative of alcoholic liver disease. In alcoholic liver disease AST is hardly>300 U/L and the ALT is usually within normal values. A low serum ALT level is caused by an alcohol-induced deficit of

pyridoxal phosphate.The transaminases are commonly not significantly raised in obstructive jaundice except in acute stage of biliary blockade due to the transport of a gallstone into the common bile duct where the transaminases can temporarily be raised upto 1000–2000 U/L limit[48,49]. Nevertheless, transaminases fall rapidly, and the hepatic function tests progress into cholestatic picture.

ENZYMES IN CHOLESTASIS

The actions of 3 enzymes are typically raised in cholestasis. They include Gammaglutamyl transpeptidase, Alkaline phosphatase and 5'-nucleotidase. GGT is sited in the endoplasmic reticulum and in epithelial cells of biliary canaliculi whereas ALP and 5-nucleotidase are present in or adjoining the biliary canalicular membrane of liver cells. GGT rise in serum is less precise for cholestasis when compared to alkaline phosphatase or 5'-nucleotidase due to its more widespread distribution in the hepatocytes.The alkaline phosphatase in serum comprises of several discrete isoenzymes present in the bone, hepatic cells, small bowel and placenta. Above the age of 60 persons may have a slightly raised alkaline phosphatase . Persons with blood groups B and O may show a rise of serum alkaline phosphatase following an oily meal because of inflow of bowel ALP into the circulation. Physiological rise is seen in adolescents and children with fast bone growth,due to bone ALP and in normal pregnancies because of entry of placental ALP.Increase in hepatic ALP is not entirely precise for cholestasis,

and smaller than threefold rise is demonstrated in nearly any kind of hepatic disorder. ALP rise more than four times seen mainly in patients with cholestatic hepatic diseases, carcinomas and amyloidosis, and Paget's disease of the bone. The liver isoenzyme is elevated in hepatic diseases.The identification of the cause of raised isoenzymes is useful, if increased ALP is the only anomalous outcome in an outwardly healthy subject .This can be advanced in numerous methods. The fractionation of the alkaline phosphatase by electrophoresis is one method. Another method is to differentiate isoenzymes by there varied susceptibility to inactivation by heat. A heat-stable fraction intensely points that either placenta or a tumor is the cause of the raised enzyme in serum. The heat labile fractions are liver, intestinal and bone ALPs. The most sensitive being bone. The measurement of serum 5'-nucleotidase or GGT is the best proven and most accessible method .In disorders other than hepatic disorders they are hardly raised. An isolated elevation of ALP of hepatic origin without icterus or raised transaminases usually indicates initial stages of cholestasis and rarely liver permeation by granulomas or malignancies[1] . Other conditions that cause a sole rise in alkaline phosphatase are Diabetes, Hodgkin's disease, amyloidosis, hyperthyroidism, inflammatory bowel disease, congestive heart failure etc.

The level of serum alkaline phosphatase elevation is not helpful in distinguishing between intrahepatic and extrahepatic cholestasis. There is essentially no difference among the values found in obstructive jaundice due

to cancer, common duct stone, sclerosing cholangitis, or bile duct stricture. Values are similarly increased in patients with intrahepatic cholestasis secondary to transplant rejection, hepatitis due to drugs, inflammatory bowel disease ,primary biliary cirrhosis and ethanol related steatonecrosis[1,2,9]. Values are also greatly elevated in hepatobiliary disorders seen in patients with AIDS (e.g., AIDS cholangiopathy due to cytomegalovirus or cryptosporidial infection and tuberculosis with hepatic involvement).

Tests centered on synthetic purposes of Liver

SERUM ALBUMIN

Hepatocytes produce and secrete 10 g of albumin per day. In patients with hepatic decompensation, albumin synthetic capacity decreases resulting in hypoalbuminemia. However, the serum albumin level also can be lowered by extrahepatic conditions such as malnutrition, enteropathy, renal disease, and hormonal disturbances. Therefore, hypoalbuminemia is not a precise pointer of liver dysfunction. As the half-life of serum albumin is nearly 20 days, the serum albumin cannot be taken as a consistent marker of liver synthetic function in subjects with acute hepatic damage. However, in subjects with chronic hepatic disease the serum albumin value is useful as a predictive marker of prognosis.

Prealbumin, like albumin, is synthesized by the liver but has a shorter half-life. Serum prealbumin levels can be influenced by several extrahepatic factors and therefore are not used widely as a marker of liver dysfunction.

SERUM GLOBULINS

Serum globulins are a heterogenous collection of proteins consisting of immunoglobulins produced by B cells, plasma cells and globulins formed chiefly in liver cells. Globulins are increased in conditions of long standing hepatic disease like cirrhosis and chronic hepatitis. In cirrhosis, the increased serum gamma globulin concentration is the result of elevated production of Ig (immunoglobulins) directed against gut bacterial flora. This occurs because the cirrhotic liver fails to clear bacterial antigens that normally reach the liver through the hepatic circulation.

Increases in the concentration of specific isotypes of globulins are often helpful in the recognition of certain chronic liver diseases. Diffuse polyclonal increases in IgG levels are common in autoimmune hepatitis; increases >100% should alert the clinician to this possibility. Raised IgM levels were found in primary biliary cirrhosis, whereas rise in the IgA levels were seen in ethanol induced liver disease.

Clotting Factors

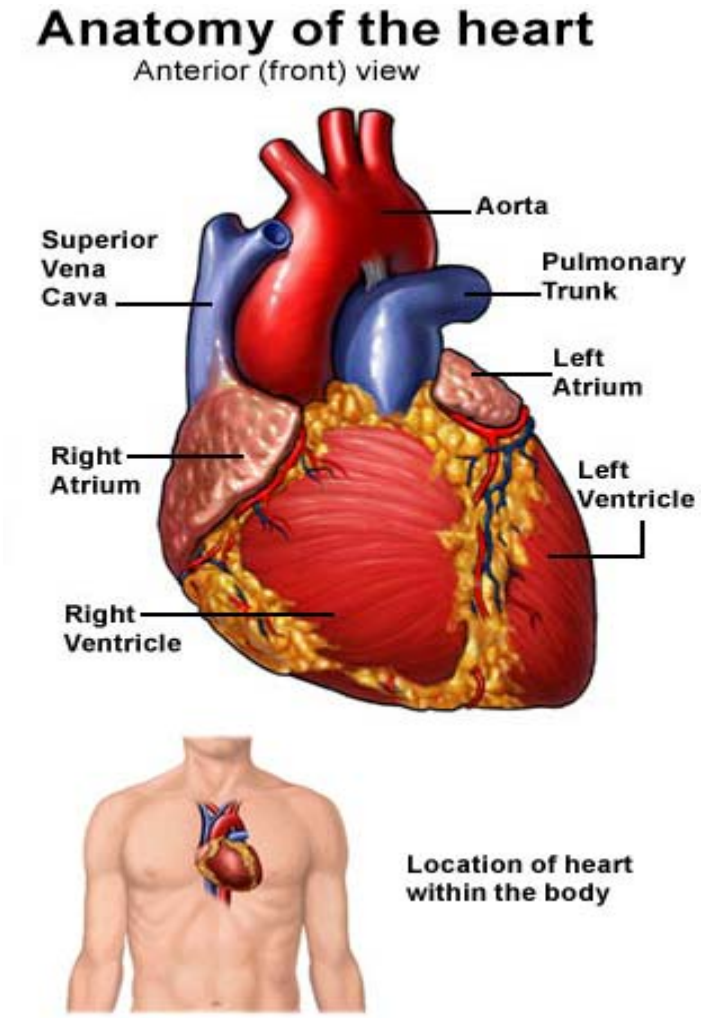
All clotting factors except factor VIII are synthesized by hepatocytes. Factor VIII is produced by vascular endothelium and reticuloendothelial cells. The prothrombin time measures the rate of production of thrombin from prothrombin. The prothrombin time provides an estimate of hepatic synthetic function because it is determined by the activity of the given factors involved

in the extrinsic coagulation pathway which includes factors II, V, VII, and X, which are all synthesized by the liver.

The differential diagnosis of an abnormally prolonged prothrombin time also includes vitamin K deficiency, therapeutic anticoagulation, and a consumptive coagulopathy. Vitamin K is needed for gamma-carboxylation and normal functioning of clotting factors 2, 7,9, and 10. Vitamin K deficiency can be associated with malnutrition, malabsorption, or antibiotic use and may lead to prolongation of the prothrombin time. The use of warfarin interferes with the vitamin K–induced gamma-carboxylation. The prothrombin time can be prolonged as a result of disseminated intravascular coagulation (DIC) and congenital deficiency of clotting factors. When prolongation of the prothrombin time is caused by liver disease, levels of factor VIII are normal or increased, whereas in DIC, factor VIII levels are decreased. Measurement of the serum factor V level and administration of vitamin K can be used to differentiate hepatic dysfunction and vitamin K deficiency as a cause of a prolonged prothrombin time. Factor V levels are decreased in liver disease but remain unaffected by vitamin K deficiency. Administration of vitamin K, 10 mg subcutaneously, results in correction of the prothrombin time by at least 30% within 24 hours in patients with vitamin K deficiency, but not in those with liver disease.

Hepatic synthetic function can be assessed in patients with acute liver failure through measurement of the prothrombin time. The level of factor 7,

which has a short half-life (6 hours) when compared to other factors, can be monitored in patients with acute liver failure to assess hepatic synthetic function .The international normalized ratio (INR), which is a reproducible method used to standardize the monitoring of anticoagulation therapy, is not superior as a prognostic indicator to the prothrombin time in patients with acute liver failure but has been incorporated into several prognostic scoring systems for assessing the severity of liver disease.



CONGESTIVE CARDIAC FAILURE

It is a clinical syndrome which may be due to a structural or functional defect of the heart causing impairment of the ventricle to receive or pump blood [4].Chronic heart failure is a systemic clinical syndrome which can have effects in other organs.The major manifestation includes tiredness,breathlessness decreasing the exercise capacity and features of volume overload like pulmonary edema and pedal edema [5].

The overall prevalence of Heart failure in the industrialized countries is two in hundred people. Incidence of heart failure rises as the age advances affecting nearly five to ten percent of population above sixty five years[1]. CHF is widely classified under two groups[1,5];

1. systolic failure (Reduced ejection fraction less than 40%)
2. Diastolic failure (Ejection fraction preserved more than 40%)

Etiology

Conditions which cause alteration in LV structure or function become predisposing factors for a patient to develop HF[5]. The leading reason for cardiac failure in developed countries in the present times is Ischaemic Heart Disease

Causes for Systolic Failure(EF less than 40%)

- Ischaemic heart disease
- Myocardial infarction
- Myocardial ischemia
- Obstructive valvular disease
- Regurgitant valvular disease
- Chronic volume overload
- Chronic pressure overloadHypertension
- Hypertension
- Non ischemic dilated cardiomyopathy
- Extracardiac and intracardiac shunting

- Inherited disorders Invasive disorders
- Injury secondary to medications and toxins
- Disorders of Metabolism
- Arrhythmias
- Infections like viral and parasitic causes

Causes for Diastolic failure (EF More than 40%)

Diseases causing hypertrophy pathologicaly

- Primary causes like HOCM(Hypertrophic cardiomyopathies)
- Secondary causes like Hypertension

Ageing

Conditions causing RCM(Restrictive cardiomyopathy)

- Invading diseases like Amyloidosis and Sarcoidosis
- Metabolic disorders like Hemochromatosis
- Disorders affecting the Endomyocardium including fibrotic conditions.

Diseases of pulmonary origin affecting heart

- Cor pulmonale
- Disorders of pulmonary vasculature

Hyperdynamic circulatory states

- Disorders of metabolism
- Hyperthyroidism
- Disordes of nutrition like Beri beri
- Increased circulatory demands

- V Shunting
- Anaemia of chronic durati

PRECIPITATING CAUSES OF CCF

- Cardiac arrhythmias
- Pulmonary embolism
- Infections, particularly lung infections
- Rheumatic or viral myocarditis
- Infective endocarditis
- Anaemia
- Conditions with increased metabolic demand like pregnancy, thyrotoxicosis
- Acute myocardial ischaema or infarction
- Accelerated hypertension
- Acute valvular regurgitation
- Severe physical work or emotional excess increase cardiac workload.
- Improper diet control
- Poor drug compliance
- Drugs worsening failure
    - Calcium channel blockers
    - Beta blockers
    - NSAIDS
    - Monoclonal Antibodies

- Antiarrhythmic drugs.
- Alcoholism

In the present study the subjects were considered as suffering from congestive cardiac failure,if they satisfied a minimum of one major and minor criteria based on the FRAMINGHAM CRITERIA for diagnosis of heart failure.

FRAMINGHAM CRITERIA FOR DIAGNOSIS OF HEART FAILURE[4,5]

Major criteria

- Paroxysmal nocturnal dyspnea or orthopnea
- Cardiomegaly
- Jugular venous distention (or CVP > 16 mm Hg)
- Hepatojugular reflex
- Rales or acute pulmonary edema
- S3 gallop
- Response to diuretic (weight loss >4.5 kg in 5 days)

Minor criteria

- Exertional dyspnea
- Nocturnal cough
- Ankle edema
- Hepatomegaly

- Pleural effusion
- Vital capacity < two thirds of normal
- Tachycardia (>120 bpm)

In this study symptomatic analysis of the subjects were done and they were classified according to the NEW YORK HEART ASSOCIATION Classification of Cardiac Failure[4,5] into 4 classes.

NEW YORK HEART ASSOCIATION (NYHA) FUNCTIONAL CLASSIFICATION

Class I

No restriction during ordinary actions

Class II

Mild restriction during ordinary actions

Class III

Marked restriction during normal actions and no symptoms at rest

Class IV

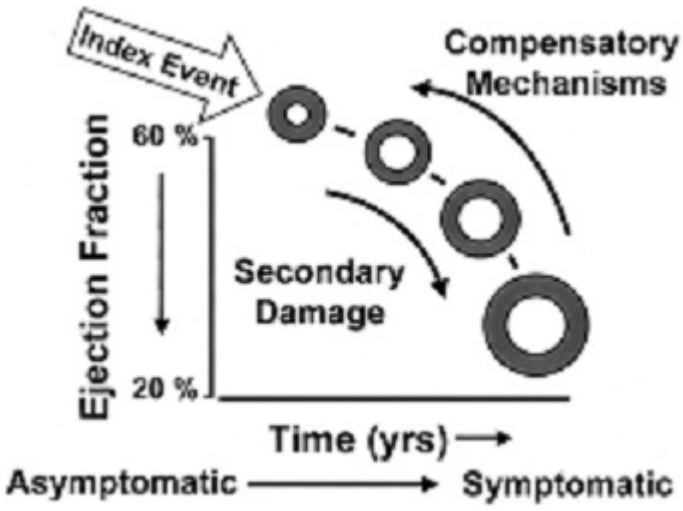
Not able to carry out physical activity without symptoms and symptoms can be present at rest

PATHOGENESIS

HF is an advancing condition started by an index event leading to injury to the cardiac musculature causing abnormal functioning of cardiac muscle cells

or interrupting the force producing capability of the myocardium, eventually disrupting the normal contracting ability of heart[6].

The inciting event can be of sudden onset (like MI) or insidious onset (like hemodynamic pressure or volume overload) or inherited (like genetic cardiomyopathies)[1,5] .Eventhough they are different in nature, ultimately they impair the pumping capacity of heart.



Cardiac failure patients seem to maintain and modify LV function for variable time ranging from months to years by means of several compensatory mechanisms which get triggered by the cardiac insult and dysfunction of left ventricle[1,4.5]. The following compensatory mechanisms are called into action

(1) The RAA axis (renin-angiotensin-aldosterone)and sympathetic nervous system activation which cause holding of salt and water and thus sustaining cardiac output

(2) raised contractile ability of myocardium.

(3) Vasodilating molecules like the ANP and BNP (atrial and brain natriuretic peptides) PGE_2 and $PGI_{2(}$ prostaglandins) and NO (nitric oxide) get activated counteracting the undue peripheral vasoconstriction.

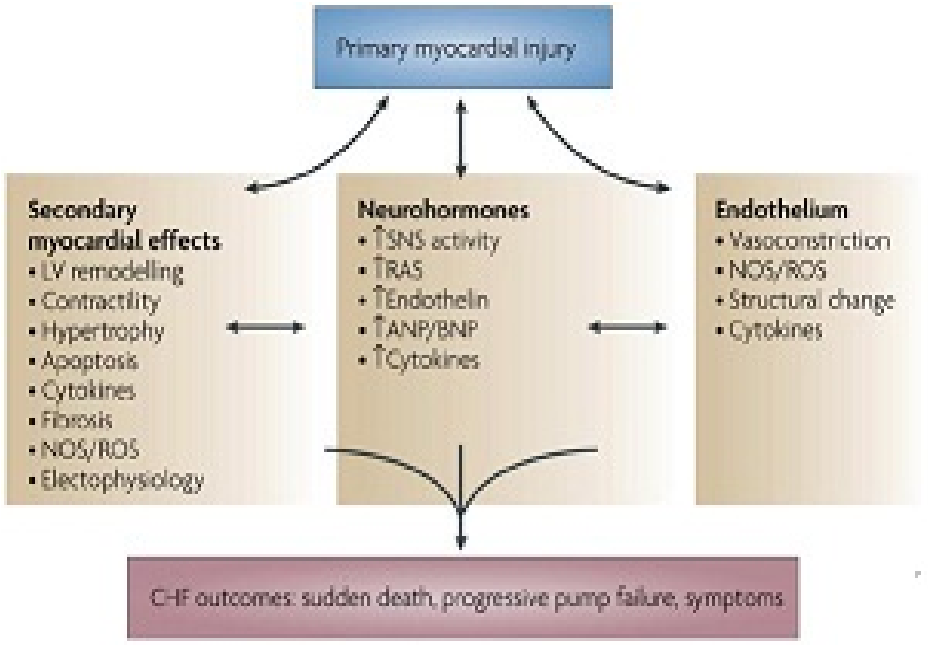
LEFT VENTRICULAR REMODELLING

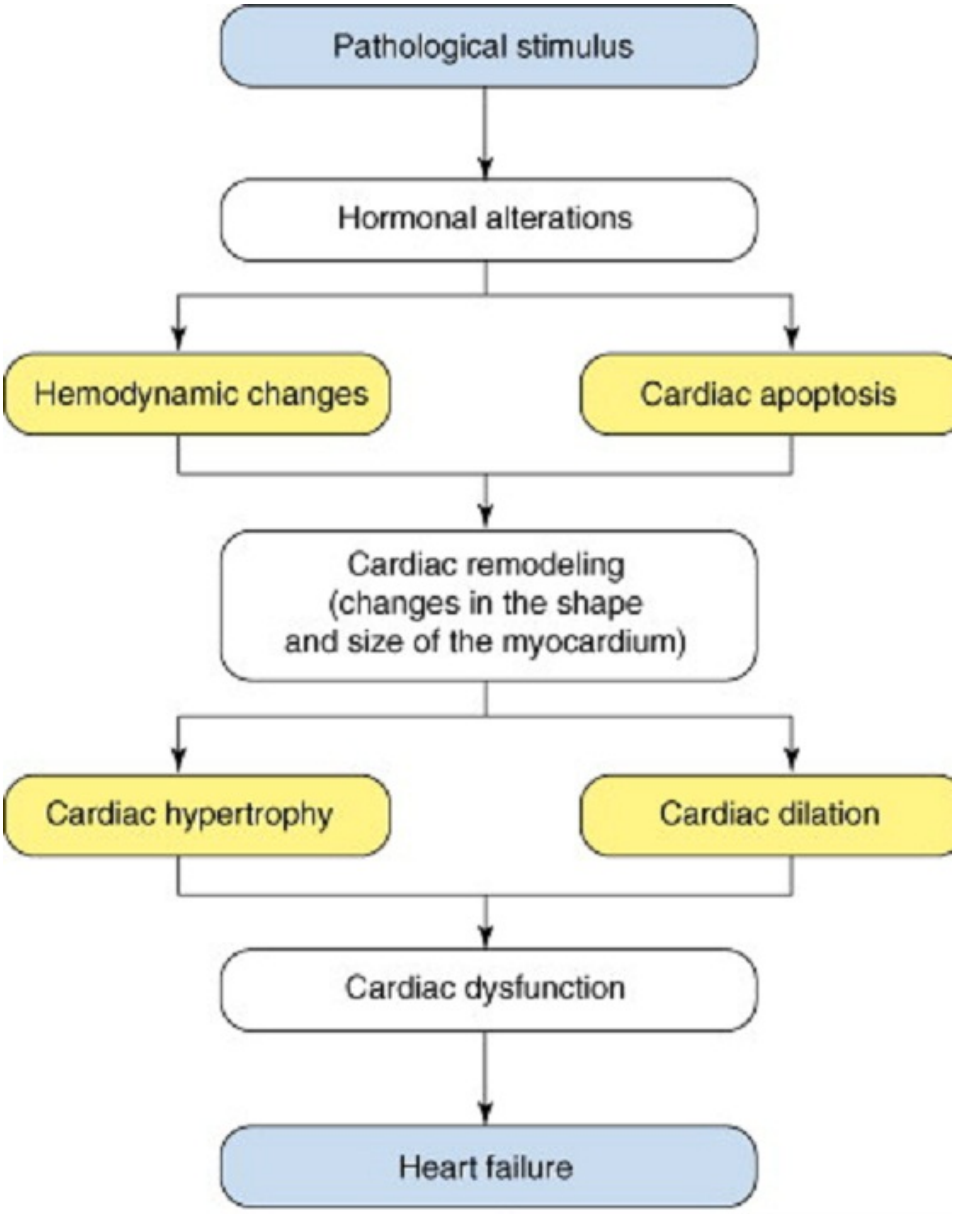
Progressive activation of the above mechanisms produce a sequence of accommodative alterations in the myocardium which is jointly mentioned as LV remodeling eventually leading to the evolution to symptomatic failure[5,6].

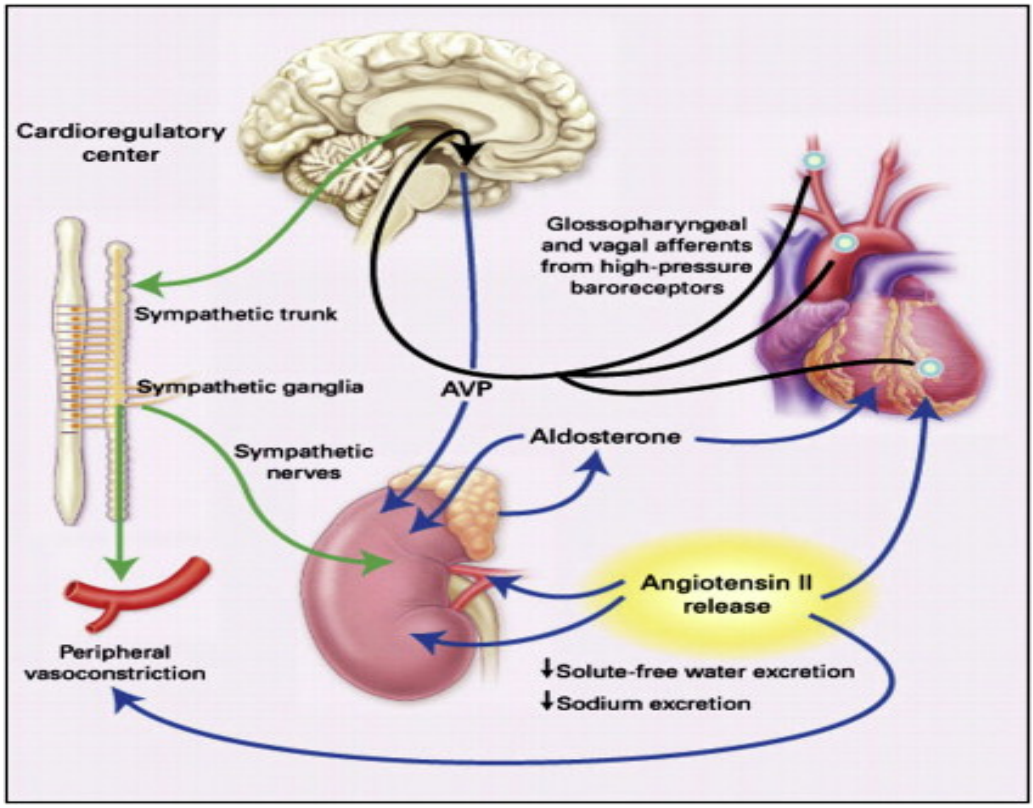
A succession of intricate events happen in molecular and cellular stages during remodeling of LV[1,5]. The factors stimulating these changes are

- Muscle fibre subjected to mechanical stretching
- Neurohormones in circulation (like noradrenaline, angiotensin II)
- Inflammatory cytokines [like TNF (tumor necrosis factor)]
- Growth factors and Peptide hormones (like endothelin)
- Oxygen free radical species (like superoxide and NO).

The persistent activation of this molecules leads to advancement of heart failure by means of the harmful effects they produce on the heart and blood vessels .


Primary myocardial injury
Secondary myocardial effects
• LV remodelling
• Contractility
• Hypertrophy
• Apoptosis
• Cytokines
• Fibrosis
• NOS/ROS
• Electophysiology
Neurohormones
• ↑SNS activity
• ↑RAS
• ↑Endothelin
• ↑ANP/BNP
• ↑Cytokines
Endothelium
• Vasoconstriction
• NOS/ROS
• Structural change
• Cytokines
CHF outcomes: sudden death, progressive pump failure, symptoms


Pathological stimulus
Hormonal alterations
Hemodynamic changes
Cardiac apoptosis
Cardiac remodeling
(changes in the shape
and size of the myocardium)
Cardiac hypertrophy
Cardiac dilation
Cardiac dysfunction
Heart failure



TYPES OF CARDIAC FAILURE

Heart failure may be acute or chronic, left-sided or right-sided, high-output or low-output, forward or backward, and systolic or diastolic[5].

Acute and chronic failure

The main characteristic feature of acute heart failure is it occurs suddenly subsequent to a large myocardial infarction or heart valve rupture . Here there is an acute fall in cardiac output leading to hypotension .There is absence of extremity oedema[4]. Chronic heart failure occurs in the context of gradually progressive dilated cardiomyopathy, valvular heart disease and systemic hypertension. Blood pressure is well preserved in chronic heart failure but usually extremity oedema is present [30].

Left-sided and right-sided failure

Left sided heart failure is characterized by pulmonary congestion causing dyspnoea and orthopnoea. Usually occurs in conditions when there is a pressure overload on LV as in aortic stenosis or it is weakened due to a myocardial infarction[1]. Right-sided failure presents with features of systemic congestion which include elevated jugular venous pressure, congestive liver enlargement and lower extremity oedema. In long- standing cases of cardiac failure like valvular heart disease (aortic and mitral valve) and hypertension, features of biventricular failure are present[4].

High-output failure and Low- output failure

High-output failure is encountered in severe anaemia, thyrotoxicosis, beriberi, arterio-venous fistulae, pregnancy and Paget's disease. The heart has to deliver excessive amount of blood to provide sufficient supply of oxygen to the highly metabolically active tissue in these conditions[6]. Low output failure is seen conditions like coronary artery disease, dilated cardiomyopathy , hypertension , pericardial and valve diseases of heart.

Forward and backward failure

Backward heart failure is featured by elevated pressure and volume in the atrium and systemic veins proximal to the failing ventricle producing sodium and water retention causing development of oedema. Forward heart failure is described based on the insufficient cardiac output as a result of left ventricular systolic dysfunction.This results in decreased renal blood flow

causing stimulation of the RAAS(renin-angiotensin-aldosterone system) with concomitant retention of salt and water producing oedema [4,5,6].

Systolic and diastolic failure

Systolic heart failure is featured by principal systolic ventricular contractile dysfunction chiefly due to myocardial dysfunction leading to an inadequate output and further symptoms. The main aetiologies include dilated cardiomyopathy , ischaemic heart disease, chronic excessive ventricular workload as in systemic hypertension, valvular heart disease (like mitral incompetence, aortic stenosis, aortic incompetence) and congenital heart disease (like ventricular septal defect, coarctation of aorta, congenital pulmonary and aortic stenosis).

Diastolic heart failure is characterized by lack of relaxation of ventricle causing rise of diastolic pressure in the ventricle and preserved diastolic volume. The commonest cause of diastolic dysfunction is ischaemic heart disease . Increased stiffness and thickening of ventricle as seen in restrictive cardiomyopathy due to amyloidosis or haemochromatosis also produces diastolic dysfunction .

In most patients with cardiac hypertrophy and dilatation, systolic and diastolic heart failure co-exist

Diastolic Heart Failure

- Small LV cavity, concentric LV hypertrophy
- Systemic hypertension

- Elderly women more common
- Normal or increased ejection fraction
- S4 gallop
- Diastolic impairment by various echo measurements
- Treatment not well established
- Prognosis not as poor
- Myocardial ischemia common

Systolic Heart Failure

- Large, dilated heart
- Normal or low blood pressure
- Broad age group; more common in men
- Low ejection fraction
- S3 gallop
- Systolic and diastolic impairment by echo
- Treatment well established
- Poor prognosis
- Role of myocardial ischemia important

Clinical Manifestations

The chief symptoms of HF are fatigue and shortness of breath. Although fatigue is thought to be due to the low cardiac output in HF, it can also be contributed by skeletal-muscle abnormalities and other non-cardiac co-morbidities[30] . In initial stages of cardiac decompensation , exertional

breathlessness is present , as failure advances lower levels of activity causes dyspnea and eventually progressing to dyspnea at rest. It has a multi-factorial origin which include pulmonary fluid collection , rising airway impedance ,declining lung compliance , anemia and breathing muscle fatigue. Dyspnea may become less frequent with the onset of right ventricular (RV) failure and tricuspid regurgitation[22].

Orthopnea

Orthopnea or dyspnea in lying down posture is late feature of failure. The cause is increased venous return to the heart in supine position leading to an increase in pulmonary capillary pressure which stimulates the juxta-capillary J receptors resulting in dyspnea. Nocturnal cough is the most frequent and common symptom. It is relieved by maintaining an upright posture. Also seen in conditions other than cardiac disorders.

Paroxysmal Nocturnal Dyspnea (PND)

It is the development of sudden onset of severe breathlessness and coughing happening usually at night-time usually 1–3 h after the patient retires to bed. It can be easily deduced from the history given by the patient which he describes as if he is awakened after a few hours of sleep by the shortness of breath and he gasps for air by standing near the window. PND manifests by coughing or wheezing and is due to increased pressure in the bronchial arteries causing compression of the airway which along with interstitial pulmonary edema leading to increased airway resistance. Patients

with PND continue to have symptoms even after assuming the erect position which differentiates it from orthopnea. Cardiac asthma is characterized by wheezing secondary to bronchospasm, and must be differentiated from primary asthma and pulmonary causes of wheezing.

Cheyne-Stokes Respiration

Cheyne-Stokes breathing is usually associated with low cardiac output. It is produced by a decreased stimulation of the central respiratory region to elevated arterial CO2 .It has the following phases: An apneic phase in which the there is a fall in the arterial PO2 and a corresponding rise in PCO2 which sensitizes the respiratory centre followed by hyperventilation and decrease in PCO2 levels which constitutes the hyperpneic phase. It is described as a brief cessation of breathing by the subject.

Other Symptoms

Patients with HF may also present with gastrointestinal symptoms. Symptoms associated with congestion of gut wall and liver are loss of appetite, nausea, early fullness and abdominal pain . Right upper quadrant pain may occur due to stretching of capsule because of congestive hepatomegaly. Cerebral symptoms, which may be due to cerebral arteriosclerosis or reduced cerebral perfusion like confusion and mood changes may occur predominantly in elderly subjects.

Physical Examination

General Appearance and Vital Signs

- In mild to moderate HF, the patient is comfortable at rest,with symptoms of orthopnoea
- In more severe HF, the patient dyspnoeic in siting posture .
- Decreased pulse pressure
- Systolic BP may be normal ,high or low according to the severity of cardiac failure
- Sinus tachycardia
- Cool peripheries , cyanosed lips and nails due to vasoconstriction
- Elevated Jugular Venous pressure
- Presence of hepatojugular reflex

Pulmonary Examination

- Pulmonary crackles due to the transudation of fluid from the intravascular space into the alveoli
- Expiratory wheezing (cardiac asthma)
- Pleural effusions result from the elevation of pleural capillary pressure and the resulting transudation of fluid into the pleural cavities.

a) pleural effusions occur commonly with biventricular failure.

b) pleural effusions are often bilateral in HF, when unilateral they occur more frequently in the right pleural space.

Cardiac Examination

- Cardiomegaly with shifted apical impulse. A sustained apical impulse due to severe LV hypertrophy
- A third heart sound (S_3) is audible and palpable at the apex due to volume overload
- A sustained and prolonged left parasternal heave due to hypertrophied right ventricle.
- A fourth heart sound (S_4) present diastolic dysfunction.
- The murmurs of mitral and tricuspid regurgitation heard in patients with advanced HF.

Abdomen and Extremities

- Tender hepatomegaly
- Pulsatile liver in systole in tricuspid regurgitation.
- Ascites
- Jaundice also occurs late with elevations of both direct and indirect bilirubin.
- Peripheral edema is usually symmetric and dependent in the ankles and pretibial region in ambulatory patients
- presacral edema and the scrotal edema in bed ridden cases.

Cardiac Cachexia

- Marked weight loss and cachexia.
- Signifies a poor prognosis.

Diagnosis of Heart Failure

Laboratory Investigations

Subjects presenting with acute heart failure or exacerbation of chronic heart disease should undergo the following regular laboratory investigations. These include

- Complete blood count
- Renal function tests
- Serum electrolytes
- Liver function tests
- Urine analysis .
- Evaluation for DM(Diabetes Mellitus) which includes fasting blood glucose,post prandial glucose and in some cases OGTT(Oral glucose tolerance test)
- Fasting lipid profile to rule out dyslipidaemia
- Thyroid function tests including TSH(Thyroid stimulating hormone)

Electrocardiogram

- A regular twelve -lead Electrocardiogram (ECG) is mandatory.
- To rule out left ventricule enlargement, arrhythmias, presence of old myocardial infarction.

A normal ECG virtually excludes LV systolic dysfunction.

Chest X-Ray

- To rule out cardiomegaly
- To assess the pulmonary vasculature,
- To find out any noncardiac reasons
- Acute cases of cardiac failure show findings of pulmonary artery dilatation and features of pulmonary congestion.
- Long standing cases of cardiac failure often lack the above radiological findings. This may be accounted by the improved lymphatic drainage of fluid in lungs.

Left ventricular function Evaluation

- ✓ The identification ,assessment and treatment of cardiac failure requires Non-invasive cardiac imaging .
- ✓ The most valuable investigation is Two-D Echo or Doppler
- ✓ It delivers a semi-quantitative evaluation of

a) Left ventricular dimensions and function

b) To find out valvular lesions

c) To identify RWMA(regional wall motion abnormalities) which suggests an old MI.

d) To look for Left atrial enlargement and Left ventricular enlargement

- ✓ Tissue and Pulse-wave Doppler beneficial for evaluation of heart failure with EF more than 40% and to identify LV Diastolic dysfunction.

- ✓ Presently MRI is the gold standard for evaluating LV dimensions and capacities giving a complete study of structure and function of heart.
- ✓ The best valuable guide to assess LV performance is Ejection Fraction(EF). Ejection Fraction=Stroke volume/ End-diastolic volume.
- ✓ Ejection Fraction(EF) is convenient to calculate using non-invasive methods and simple to understand.
- ✓ The major shortcoming of EF is it is easily affected by variations in end diastolic volume and vascular resistance.

Biomarkers

- ➢ Natriuretic peptides in circulation are valuable markers in identifying people with HF.
- ➢ B-type natriuretic peptide (BNP) and N-terminal pro-BNP are fairly sensitive indicators for detecting heart failure with depressed EF
- ➢ A lesser degree of elevation noted in heart failure cases with maintained EF.
- ➢ Levels of Natriuretic peptide rise with age and kidney damage.
- ➢ Additional Biomarkers are
    a) Troponin T and I
    b) C-reactive protein
    c) TNF receptors
    d) Uric acid

Exercise Testing

- Treadmill or bicycle exercise testing valuable for evaluating the requirement of heart transplantation in severe advanced HF .
- A greatest oxygen uptake (V_{O2}) <14 mL/kg / min was found to have a bad prognosis.

Cases with V_{O2}<14 mL/kg /min were found to have prolonged survival with transplantation .

Differential Diagnosis

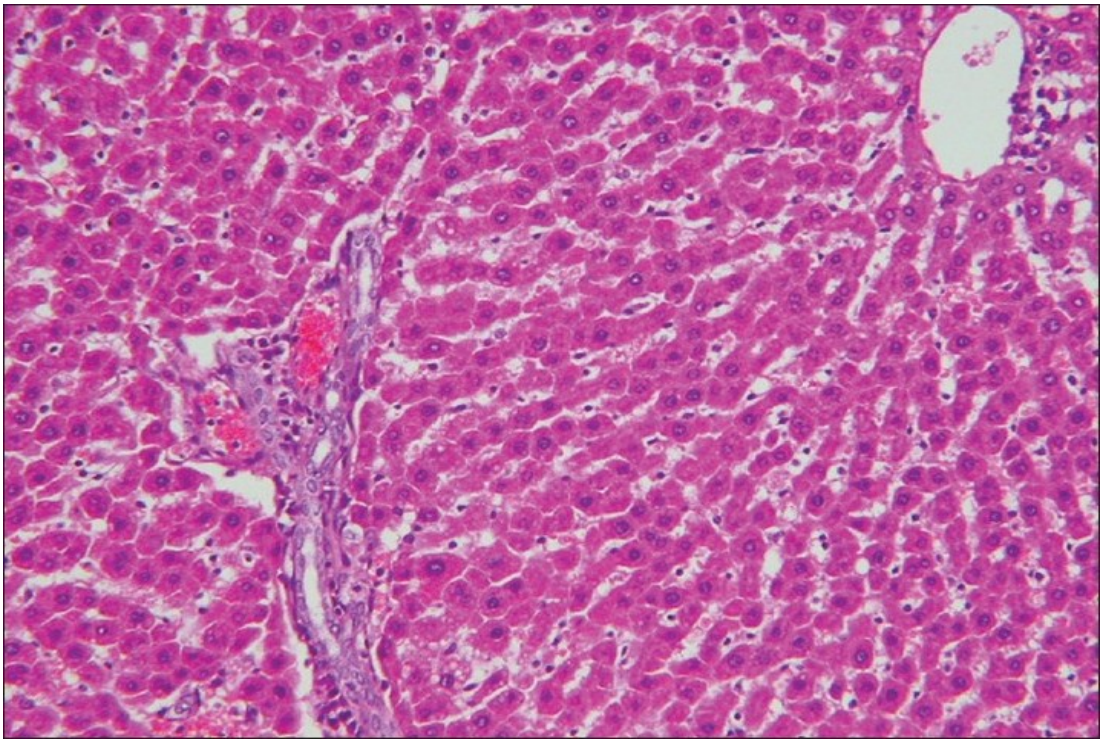
Following conditions should be considered in differential diagnosis of cardiac failure

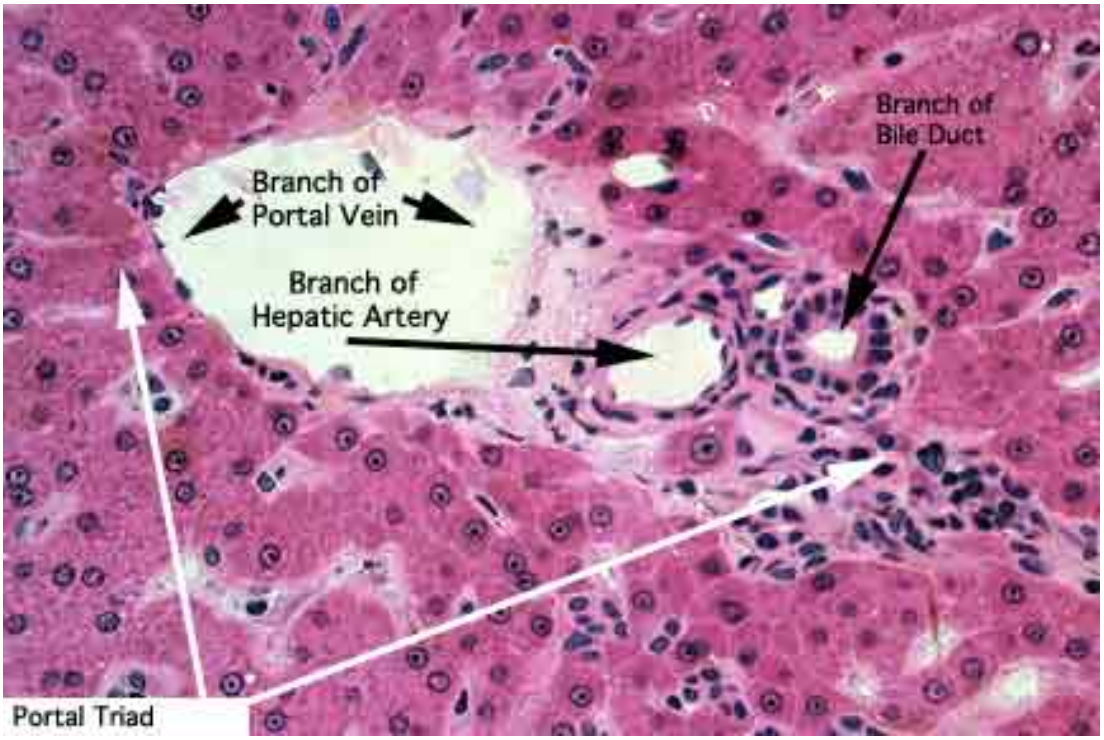
(1) Kidney Failure

(2) Noncardiogenic pulmonary congestion like ARDS(acute respiratory distress syndrome).

The diagnosis of cardiac failure is direct in the presence of typical clinical features. But at times there may arise difficulty in differentiating cardiac dyspnoea from respiratory causes. In such situations noninvasive cardiac imaging, biomarkers, pulmonary function testing become valuable.

NORMAL HEPATIC ARCHITECTURE





MECHANISM OF HEPATIC DYSFUNCTION IN HEART FAILURE

Heart failure causes:

a) reduced liver blood supply

b) elevated hepatic venous pressure causing swelling of sinusoids and atrophy of liver cells.

In cardiac failure there is elevated venous back pressure which is transferred to the hepatic veins and results in congested liver[22].Another major factor causing injury is hypoxia[23.] Histological analysis shows atrophy of liver cells in zone 3 is caused by raised pressure[24].

Raised venous pressure in the sinusoids cause widening of sinusoidal pores leading to leakage of fluid into perisinusoidal space [25].This edema decreases transport of nutrients and oxygen to the liver cells[24]. Usually this fluid drains into lymphatics ,when there is excess fluid more than the drainage ability of lymph channels this fluid with excess protein content collects in the peritoneal cavity and produces ascites[26.] When the congestion becomes chronic fibrosis ensues in zone 3 ,surrounding the veins and perisinusoidal space and reduce transfer of nutrients to liver cells. Long standing venous stasis can promote thrombus formation in sinusoids and venules which has fibrogenic tendency leading to regional fibrosis in liver.

Reduced blood supply to liver is also important in causing necrosis of cells as observed by Sherlock et al .Wanless et al as described in their

study that acute left heart failure led to necrosis of zone 3 liver cells in the absence of right heart failure showing that cardiac output is a major factor causing hepatic injury. Still congestion appears to be a cofactor in hepatic injury. It plays an important role in preparing the liver sensitive to ischaemic insults.

Liver ischaemia

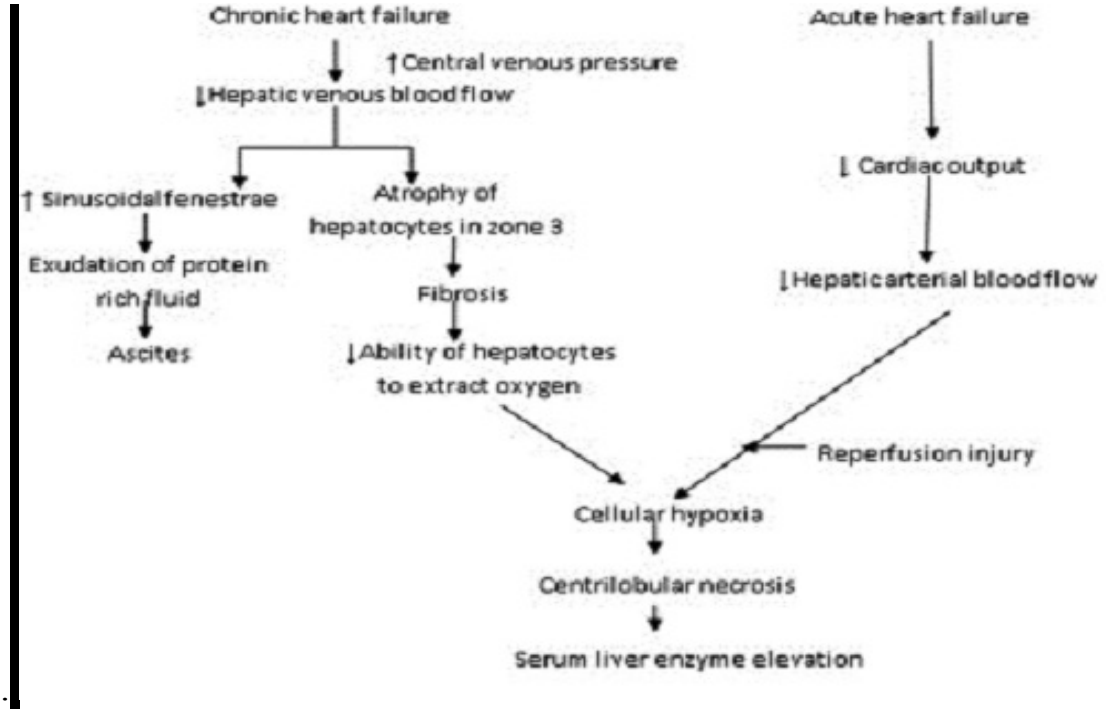
Disparity between liver oxygen supply and need leads to liver ischaemia. As liver has a constant metabolism ,oxygen delivery is the major determinant of liver ischaemia[26].Oxygen supply to liver depends on the hepatic blood flow and oxygen content of blood. It has been shown that cardiac output determines the blood supply to the liver .Hepatic blood supply is dual .Liver receives 20% of blood supply from hepatic artery and 80% from portal vein,hence major oxygen supply is from the portal vein.

With exercise usually cardiac output increases but in diseased heart cardiac output fails to rise and there is a fall in hepatic blood supply.In the normal state liver cells compensate by increasing the oxygen extracted.But in conditions of stress liver metabolic demands increase and oxygen extraction cannot be increased above a limit leading to liver cell hypoxia in the zone 3 of acini [27].

Observation in animals show that liver cells are susceptible to reduced oxygen supply at physiological temperatures due to increased metabolism than other liver cell types[28]. Nutrition also plays significant role in

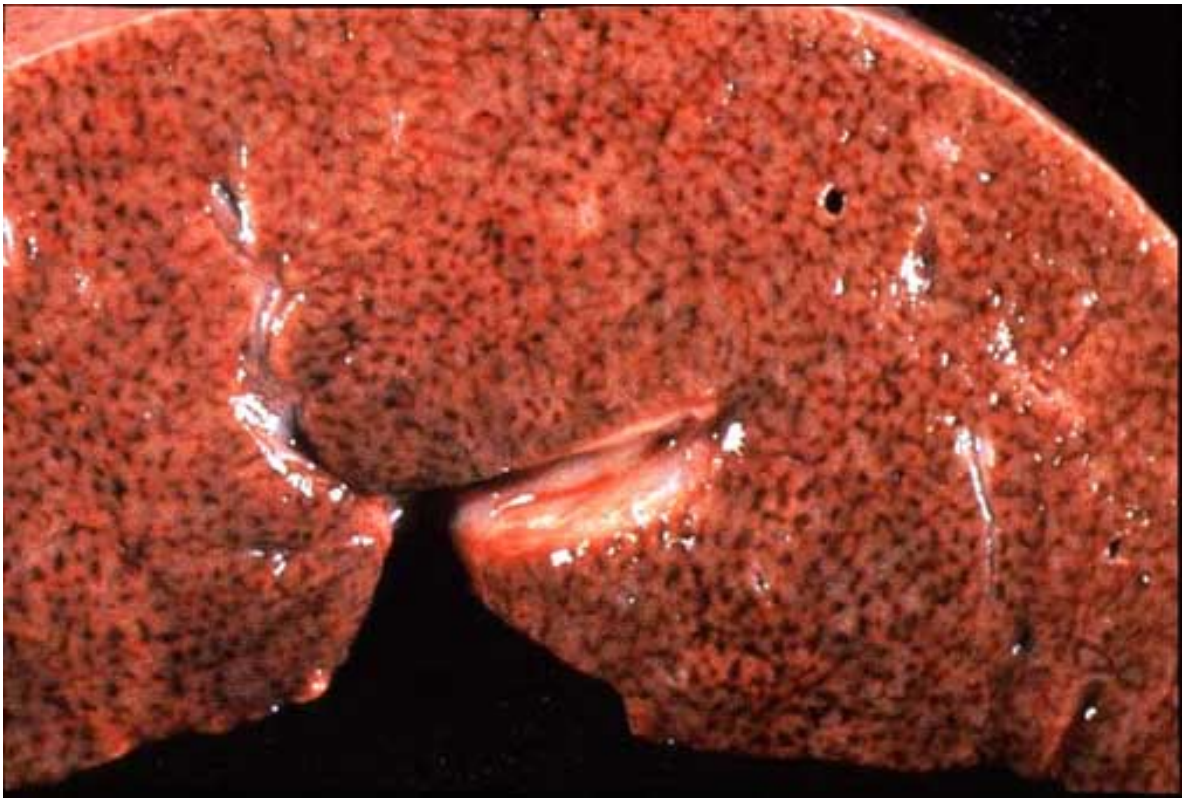
determining liver cell sensitivity to hypoxia . Ishaemia to liver cell causes damage to mitochondria ,decrease in ATP,increase in intracellular calcium and protease activation [29]. Reperfusion injury also causes damage to liver cells by formation of free radicals and lipid peroxidation.

In the damaged mitochondria reactive oxygen species are formed which has direct toxic effect on the cells.Reperfusion causes transcription of numerous genes in liver cells that produces factors and various cytokines leading to liver cell damage .



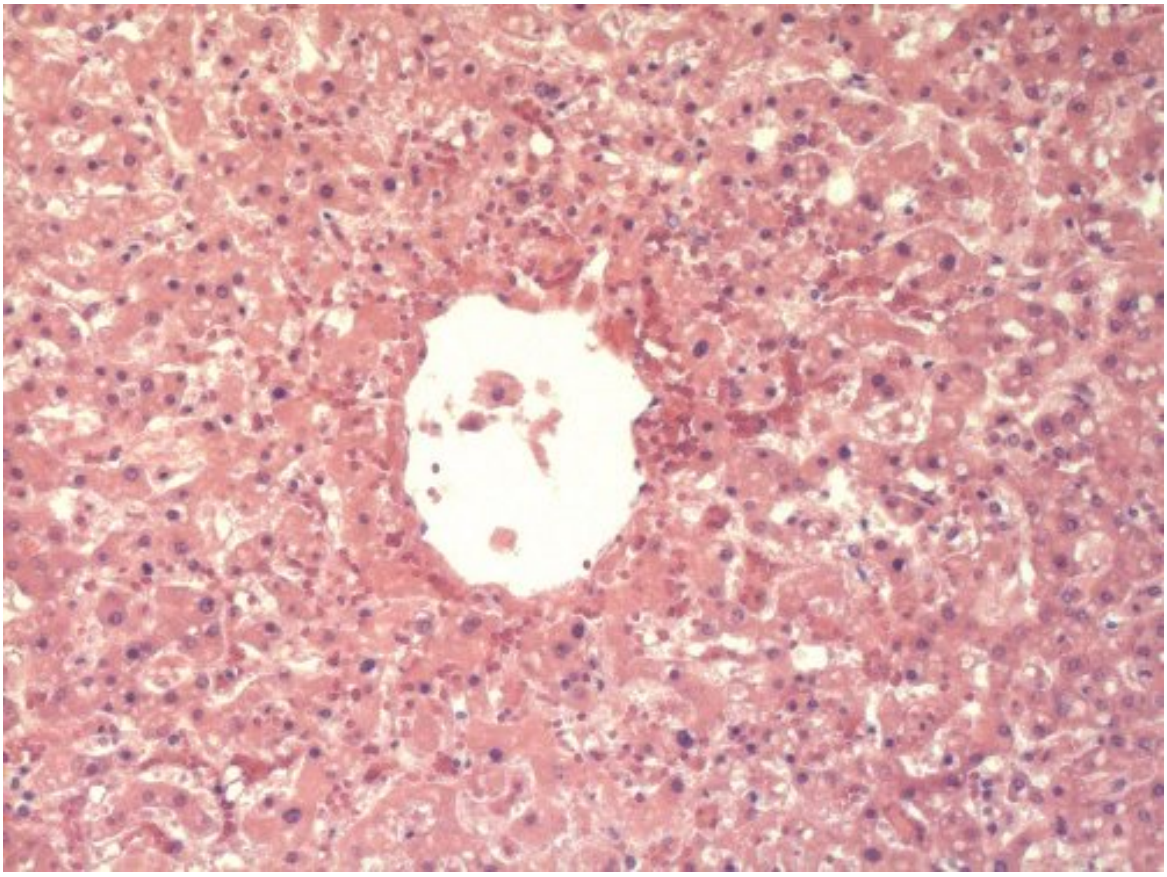
HIOSTOPATHOLOGY OF LIVER IN CONGESTIVE HEART FAILURE

Macroscopic appearance



In congestive heart failure the size of liver is enlarged ,surface is smooth and the edges are rounded with purple coloured appearance.Cut section of liver shows venous engorgement with characteristic nutmeg appearance [7]. The pale periportal region is seen alternating with the dark brown centrilobular region. In later stages when cardiac fibrosis ensues the capsule becomes granular and uneven. Cross section of liver revealing ill defined granular parenchyma and presence of nodules in the periportal regions[9] .The size of nodules being less than 1-2 mm.When compared to true cirrhosis nodular size is less , ill defined, non uniform distribution and situated in the periportal regions[7] .

Microscopic appearance



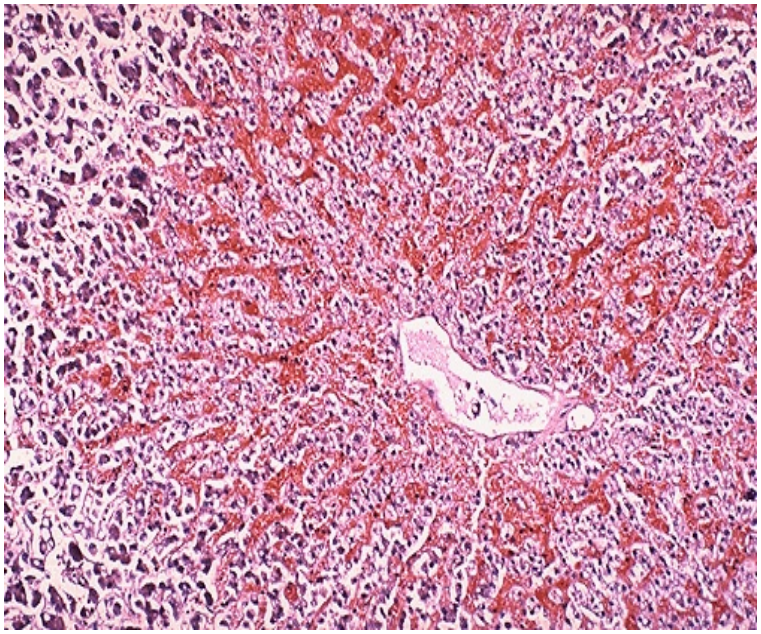
Liver in cardiac failure shows microscopic features of congestion and necrosis in zone3 .In initial stages of congestion the zone 3 liver cells are flattened and atrophic and the nearby sinusoids are filled with blood. As the severity of congestion increases more significant atrophic changes are noted with further extension into the veins[9] .Hepatocytes in centrilobular zone shows large concentrations of brown pigment.

Later on there is development of fibrosis across the central veins . Reduction in cardiac output and decreased blood flow leading to hypoxia is main reason for zone 3 necrosis.It has been reported that necrosis can occur

even without shock or hypotension.An associated inflammatory reaction is noted with presence of lymphocytes ,neutrophils and plasma cells.

Peripheral zones show a rise in the liver cells leading to degenerative hyperplasia. This causes liver cell plate thickening. The cells are large with pale cytoplasm and pleomorphic nuclei. Certain cases show nodular hyperplasia.

The predominant histological features are central portal fibrosis with early nodularity in the parenchyma. Cardiac cirrhosis is reported to be a rare occurrence[21].



Hepatic Congestion:

There is dilatation of the central veins, sinusoids and peri-sinusoidal space leading to pressure atrophy of the liver cells which eventually necrose producing central hemorrhagic necrosis. Ischemic mechanisms can also need

to necrosis. Fatty changes are also seen in certain liver cells. Zone 3 hepatocytes show a light brown pigment which is lipochrome[23].

CLINICAL FINDINGS IN CONGESTIVE HEPATOPATHY:

Most leading cause of congestive heart failure producing liver abnormalities in the developed world is coronary artery disease. Incidence of hypertension is also increasing. Rheumatic heart disease leading onto cardiac failure which was previously more common has declined. Other uncommon causes are cor pulmonale, cardiomyopathies and congenital heart diseases. Hepatic abnormality in cardiac failure is usually asymptomatic and mild. Routine liver function tests may show abnormality in these patients. Clinically patients can have right hypochondrial pain due to enlargement of liver and stretching of the capsule. Other symptoms like anorexia, vomiting can also occur[11,12]. Usually acute heart failure or exacerbation of chronic heart failure presents with such symptoms.

Physical Examination:

Jaundice is reported in nearly 20% of patients with congestive hepatopathy. Hepatomegaly is noted in 90-95% of patients presenting with severe cardiac failure. The liver may be enlarged upto 5 cm beneath the costal margin in nearly 50% of the subjects. JVP is elevated and hepato-jugular reflex can be seen. Pulsatile liver can be visualized in cases with tricuspid insufficiency. Ascites is observed in approximately 10-40% of the cases.

Pedal edema and pleural effusion has also been reported in patients with right heart failure.

LIVER BIOCHEMICAL ABNORMALITIES IN HEART FAILURE

Serum Bilirubin:

A wide range of liver function abnormalities has been noted in congestive cardiac failure. Nearly 75% of patients show a slight elevation in serum bilirubin values. Usually it does not exceed 3mg/dl and the indirect fraction is more than direct fraction. Factors producing this rise include liver cell dysfunction, RBC lysis, pulmonary infarction, infections and drugs. Sherlock et al observed a relation between right atrial pressure and serum bilirubin in his study. Hence the jaundice in right heart failure occurs predominantly due to congestion than ischemia. With the control of failure the bilirubin values become normal in a period of 1 week.

Serum Transaminase:

These enzymes show a rise in congestive cardiac failure. AST and ALT show an increase in nearly 30% of cases whereas LDH was found to be increased in 50% of cases.

Reduced liver blood supply and venous congestion lead to increase in transaminases, however the predominant factors are hypoxia and necrosis. In a study of 175 cases with both acute and chronic failure, AST showed a predominant increase in acute heart failure than chronic cases. The values

were in the range of 40-90 IUs. The rise in ALT values were less significant. In cases of acute severe cardiac failure with hypotension and shock, AST levels as high as 1000-10000 IUs were reported. The rise in AST, ALT and LDH is in accordance with the rise in venous pressure, PCWP (pulmonary capillary wedge pressure) and cardiac output.

A recent occurrence of acute heart failure, already existing chronic heart failure and early onset of renal dysfunction suggest that hepatic dysfunction is due to circulatory failure and not due to viral or drug induced causes.

Serum Alkaline phosphatase:

In most cases of cardiac failure, ALP levels are within normal range. In certain studies an elevation of 10-20% has been reported. The rise in ALP values shows no relation with serum bilirubin or transaminases. In cases with massive hepatomegaly high values have been observed. Hence intrahepatic blockade secondary to congestion is considered to be the cause for abnormal levels. With the control of cardiac failure raised values become normal in nearly 1 week.

Serum proteins:

In congestive hepatomegaly 30-50% of patients were reported to have reduced serum albumin levels. This reduction showed no correlation with the duration of cardiac failure. The values were in the range of 2.5-2.9 g/dl. The causes for decreased albumin in cardiac failure are reduced synthesis,

reduced absorption and poor nutrition. The values rarely go below 1.5 g/dl. The correction in serum albumin following control of cardiac failure takes a few months.

Increase in globulin was observed in 40-60% of cases with right heart failure. It is more common in acute rather than chronic failure. Usually a mild rise noted with values ranging from 3.5-4.1 g/dl in most of the cases. This increase was not found to return to normal even after control of heart failure.

Prothrombin time:

It is a sensitive marker of right heart failure as it was found to be prolonged in nearly 90% of subjects with congestive hepatomegaly due to cardiac failure. This prolongation may be due to reduced liver production or decreased Vitamin K dependent activation of clotting factors. Following treatment of right heart failure it takes two to three weeks for the resolution of prothrombin time.

Long-standing and recurrent congestive cardiac disease can produce cardiac cirrhosis. However the incidence is very low as most patients succumb to cardiac illness before the onset of cirrhosis.

REVIEW OF JOURNALS AND PAPERS

Liver enlargement is considered as one of the common presentation of congestive cardiac failure. A large number of studies on liver function have been conducted by many investigators to assess the extent of liver damage in heart failure.

It was Kierman[29] who first found an association between pathology of liver and congestive cardiac failure.He was the one who elaborated the term nutmeg liver.Later on after nearly seventy years Mallory gave the description of the characteristic microscopic appearance of congested liver with focal necrosis and centrilobular congestion[13]. Investigators like Lambert et al , Zimmerman et al observed the fatty alterations and exudation of fluid into pericapillary space causing pressure over the capillaries[15,19].

In cardiac failure patients the biochemical and pathological findings of necrosis in zone 3 of hepatic acini was elaborated by Sherlock et al [12.]. Subjects suffering from severe cardiac failure were found to have elevated bilirubin levels by Cantarow and Jolliffe et al who observed reduced clearance of bromsulfalein from circulation in cardiac failure cases[12,14]. Studies conducted in Montefiore medical centre also reported similar observations. Cardiac failure cases showed a three fold increase in the fibrotic changes in liver when compared to cases without cardiac decompensation. Gravin et al has reported cases of cardiac cirrhosis in autopsy findings of patients whose principal cause of death was heart failure[21].

Studies conducted by Rich et al , Libman et al reported increased incidence of jaundice in cardiac failure secondary to pulmonary embolism and infarction [18,20]. Other theories proposed in the pathophysiology of hepatic dysfunction include presence of sepsis as observed by Mallory et al[13], hypoxia occurring due to lack of nutrition as noted by Keefer et al[17] and Jaffee et al[16] studied

the role of compression on liver dysfunction. Killip et al reported in his study the enormous rise in serum aminotransferases in cases with shock[36]. All the above data point towards the association between liver function abnormalities and heart failure.

MATERIALS AND METHODS

PLACE OF STUDY

This study was conducted in the General Medical wards and Intensive care unit of Tirunelveli Medical college hospital,Tirunelveli.

PERIOD OF STUDY

November 2011 to November 2012.

DESIGN OF STUDY

This study is a Single Centre Cross-Sectional and Analytical Study. A total of 60 subjects were included in this study.

METHODOLOGY

A) SUBJECT SELECTION

1) Inclusion criteria

1.Congestive cardiac failure in all age groups of varying etiologies

2) Exclusion Criteria

1. History of alcoholism.
2. Past history of jaundice.
3. Recent intake of hepatotoxic and cholestatic drugs.
4. Presence of viral markers
5. Blood transfusion.

All subjects included in this study were subjected to thorough clinical examination. All were subjected to laboratory investigations as per the proforma.

The following liver biochemical tests were carried out in this study:

1. Serum bilirubin
2. Serum transaminases
3. Serum alkaline phosphatase
4. Serum proteins
5. Prothrombin time

Serum Bilirubin:

Estimation of serum bilirubin was done by the Wandenburg reaction. In this test the bile pigments are diazotized by the sulphalinic acid and the products are estimated calorimetrically. This reaction can also differentiate indirect and direct fractions due to the differing solubilities of these fractions. The water soluble direct fraction produces the direct VB reaction when carried out in an aqueous medium. In ethanol the intramolecular hydrogen bonds of indirect bilirubin are fragmented and both direct and indirect fragments show reaction giving the total bilirubin value. The direct bilirubin I subtracted from the total bilirubin to get the indirect bilirubin value.

Serum enzyme assays:

Serum AST and ALT:

In this study AST and ALT was measured by enzymatic substrate method. AST and ALT substrates along with dinitro phenyl hydrannel were used. The enzyme catalyses the exchange of gamma amino group of alanine

to the gamma keto group of glutamate forming oxalo-acetic acid and pyruvic acid.

Serum ALP:

A variety of assays have been developed to measure alkaline phosphatase using different substrates. The substrates used were aminoantipyrine solution, alkaline phosphate buffer, potassium ferricyanide and substrate. Increased levels of ALP shows biliary tract dysfunction. Slight to moderate elevation in ALP activity can occur in congestive cardiac failure. The raised levels signify rise in the synthesis of ALP by liver cells and biliary epithelium.

Serum Proteins:

Widespread hepatic damage leads to reduction in serum levels of fibrinogen, prothrombin, albumin and other proteins which are produced exclusively by the liver cells. The estimation of serum proteins signify hepatic synthetic function. The most major protein synthesized by the liver is albumin. Normal level ranges from 3.5-5.5 mg/dl. It has a long half-life i.e 14-20 days and daily turn-over is less than 5%. Hence it is not an accurate indicator of acute hepatic damage.

Serum globulins include alpha and beta globulins as well as immunoglobulins. Normal value is 2-3.5 mg/dl. Hyperglobulinemia occurs secondary to activation of the reticulo-endothelial system in response to the antigens presented passing through the liver.

Serum proteins are estimated by Biuret method. Substances which contain 2 or more peptide bonds and CO-NH2 groups give a purple or blue coloured precipitate with alkaline copper solution. Different proteins give differing amount of colour which helps in distinguishing them by this reaction.

Prothrombin time:

Clotting factors like fibrinogen, factor 2,5,7,9,10 are synthesized in the liver. Any dysfunction of the clotting factors can be determined by one stage prothrombin time. This method calculates the conversion rate of prothrombin to thrombin in the presence of calcium and thromboplastin. This reaction requires properly functioning Vitamin K dependent clotting factors. These clotting factors have a short half-life, hence prothrombin time can be taken as an earlier marker of hepatic injury and its prolongation in both acute and chronic hepatic damage signifies worse prognosis.

NORMAL VALUES OF LIVER FUNCTION TESTS

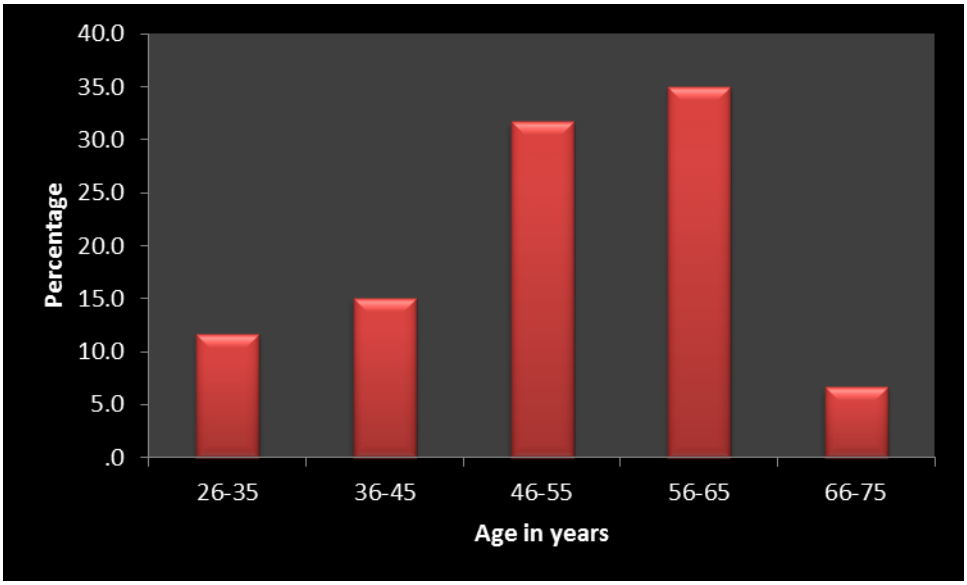
SL NO	LIVER FUNCTION TESTS	NORMAL VALUES
1.	Serum BILIRUBIN	0.3 – 1.2mg/dl
2.	Serum AST/SGOT	0 – 40 I.U
3.	Serum ALT/SGPT	0 – 35 I.U
4.	Serum ALP	20 – 140 I.U
5.	Serum TOTAL PROTEINS	6 – 8.5 g/dl
6.	Serum ALBUMIN	3.5 – 5.5 g/dl
7.	Serum GLOBULIN	2.5 – 4.5 g/dl
8.	PROTHROMBIN TIME	12 – 14 sec (control) abnormal if >1.5 times

OBSERVATION AND ANALYSIS

TABLE 1 - AGE DISTRIBUTION OF THE CASES

Age group of the cases in years	Frequency of cases in each age group	percentage
26-35	7	11.7
36-45	9	15.0
46-55	19	31.7
56-65	21	35.0
66-75	4	6.7
Total	60	100.0

AGE DISTRIBUTION



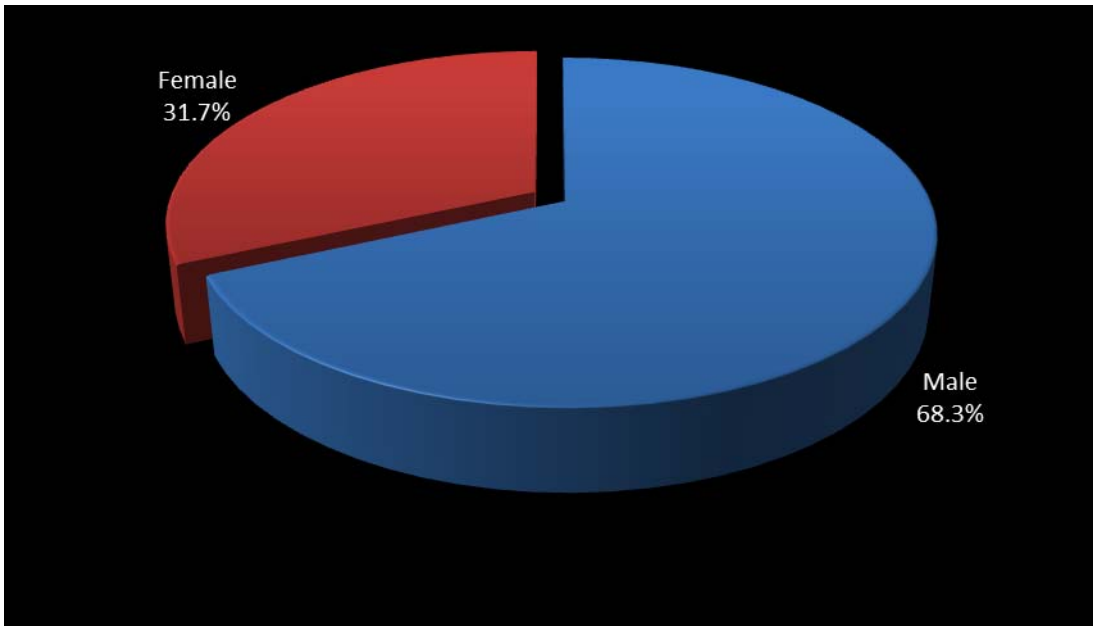
Out of 60 subjects studied 19 cases belonged to the age group 46-55yrs and 21cases belonged to the age group of 56-65 yrs showing the rising prevalence of cardiac disease with advancing age.

TABLE 2

SEX DISTRIBUTION OF THE CASES

Gender group of cases	Frequency of cases in each group	Percentage
Male	41	68.3
Female	19	31.7
Total	60	100.0

SEX DISTRIBUTION OF CASES



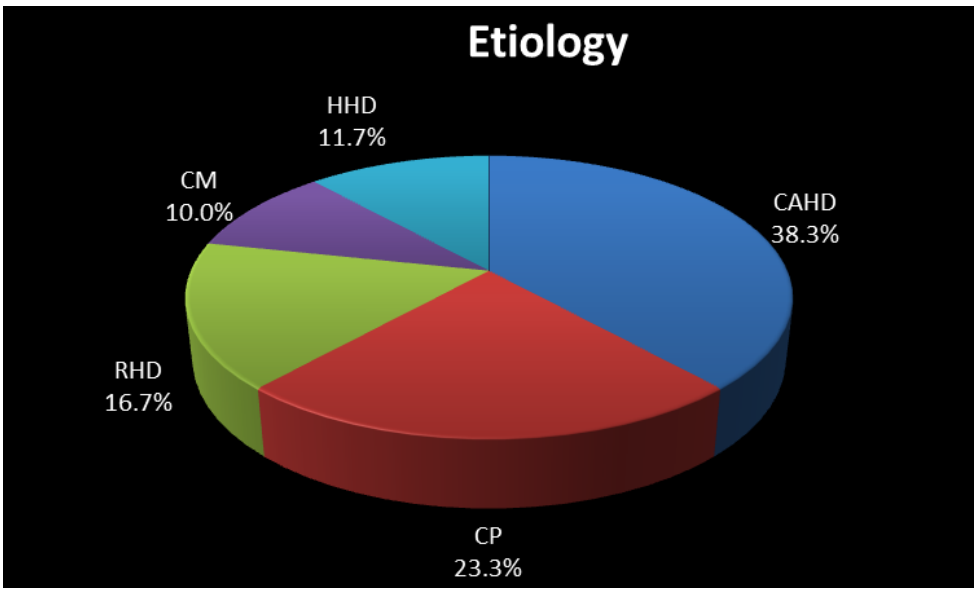
In this study 60 subjects were chosen randomly,of these 41 were males which is 68.3% and 19 were females which is 31.7% suggestive of the rise in cardiac diseases and failure in male population.

TABLE 3

ETIOLOGY OF CARDIAC FAILURE

Etiology of failure	Frequency of cases	Percentage
Coronary artery disease	23	38.3
Cor Pulmonale	14	23.3
Rheumatic heart disease	10	16.7
Cardiomyopathy	6	10.0
Hypertensive heart disease	7	11.7
Total	60	100.0

ETIOLOGY OF CARDIAC FAILURE

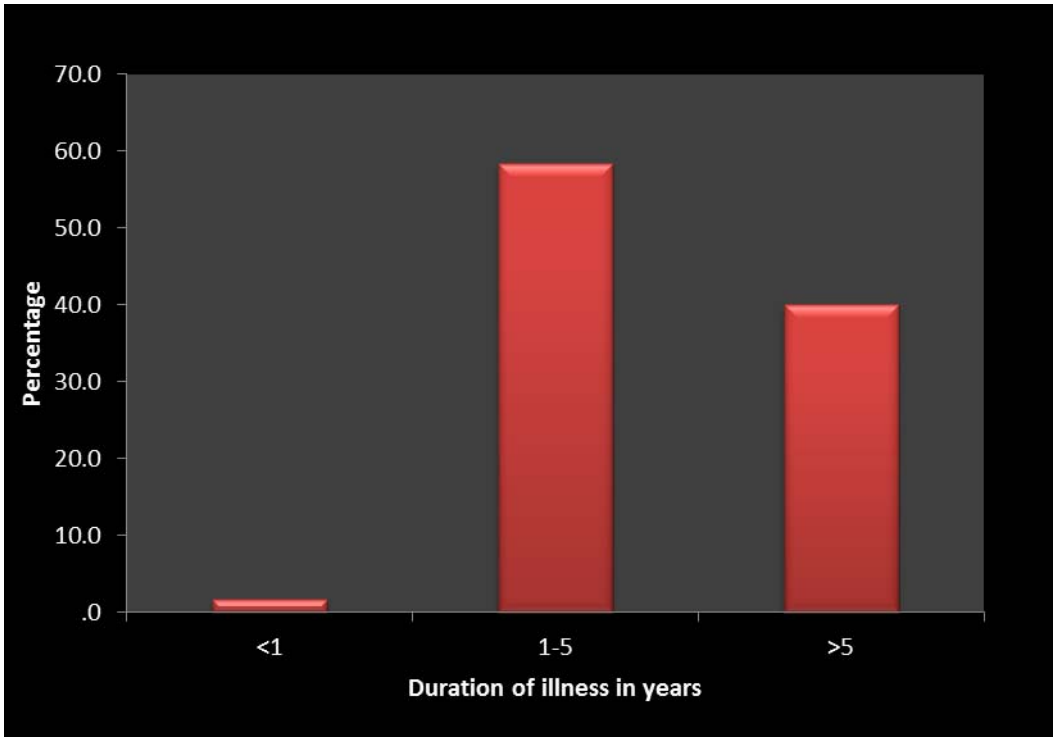


Maximum number of cases(38.3%) came under the category of Coronary Artery Disease followed by Cor pulmonale (23.5%). This shows that Coronary artery disease is emerging has the single most common cause of cardiac failure. The incidence of Rheumatic Heart Disease which was previously considered as leading cause of heart failure has declined.

TABLE 5

DURATION OF CARDIAC FAILURE

Duration of cardiac failure	Frequency in each group	Percentage
<1	1	1.7
1-5	35	58.3
>5	24	40.0
Total	60	100.0

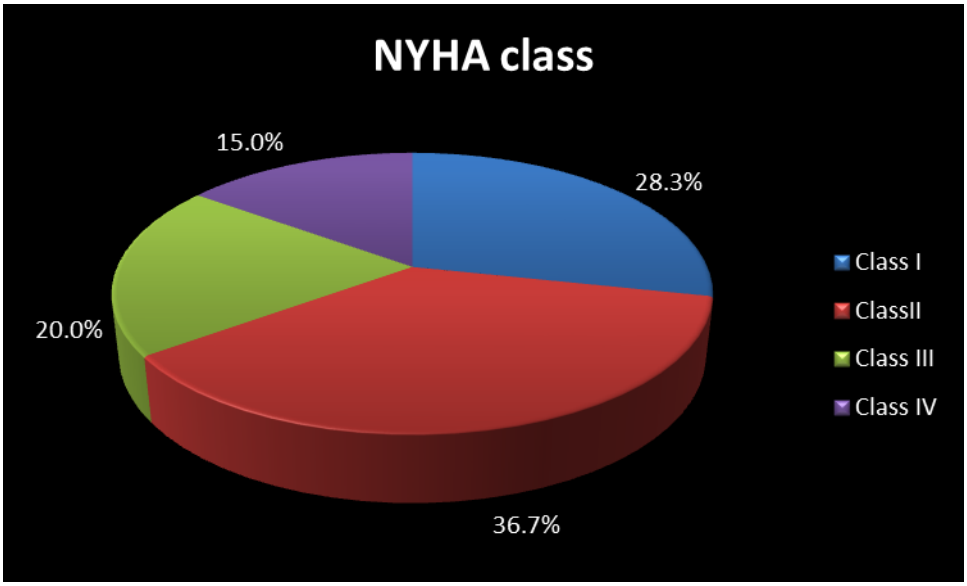


Of the 60 subjects studied ,the duration of illness is between 1- 5 years in 35 cases ,less than 1 year in 1 case and more than 5 years in 24 cases.

TABLE 4

CASE DISTRIBUTION ACCORDING TO NEW YORK HEART ASSOCIATION CLASS OF HEART FAILURE

NYHA class of heart failure	Frequency of cases in each class	Percentage
Class I	17	28.3
ClassII	22	36.7
Class III	12	20.0
Class IV	9	15.0
Total	60	100.0

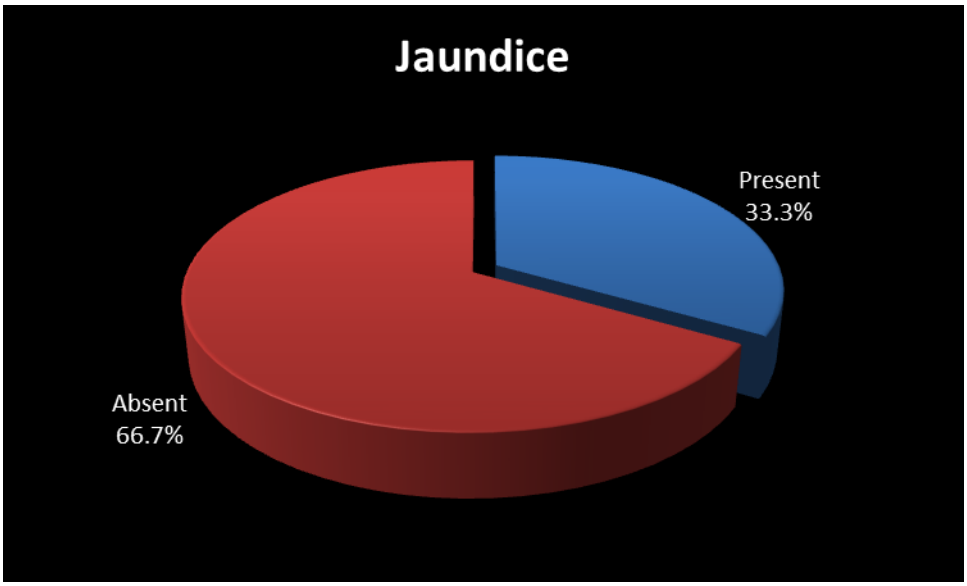


Of the total 60 subjects 17 cases belonged to class1 ,22 cases belonged to class2,12 belonged to class3 and 9 belonged to class 4.This suggests the improvement in the control of failure symptoms with the currently available therapy.

TABLE 6

PRESENCE OF CLINICAL JAUNDICE IN THE CASES

Presence of jaundice	Frequency	Percentage
Present	20	33.3
Absent	40	66.7
Total	60	100.0

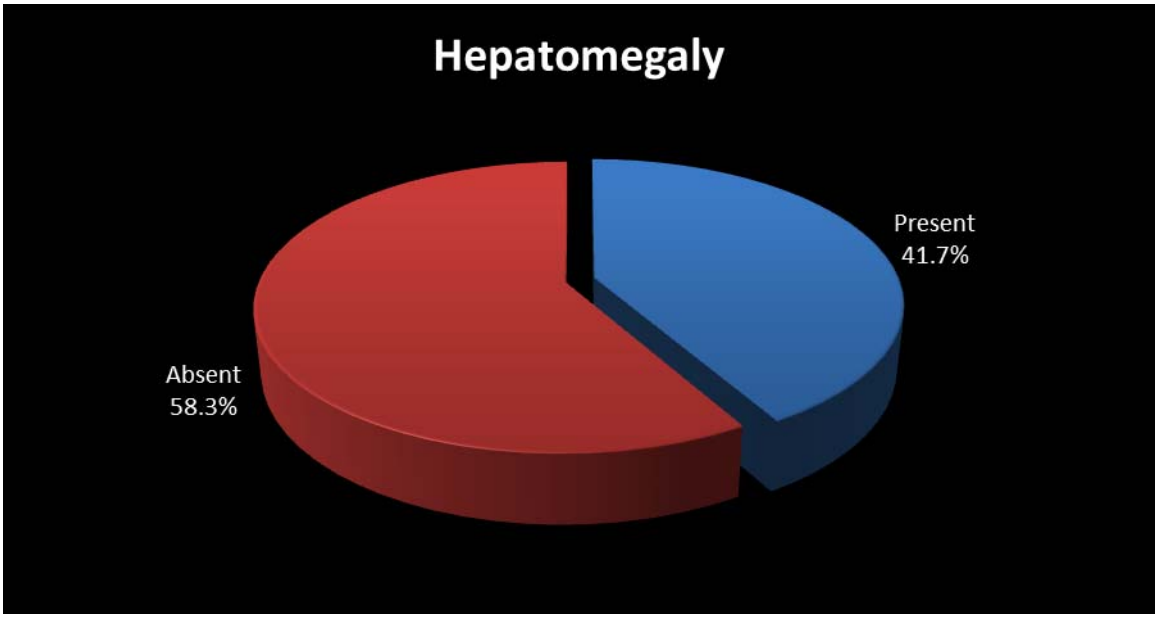


Clinical Jaundice was detected in 20 cases which constitute 33.3% and the rest were found to be normal which correlates with the pbservation of Biegus et al.

TABLE 7

PRESENCE OF HEPATOMEGALY IN THE CASES

Presence of Hepatomegaly	Frequency	Percent
Present	25	41.7
Absent	35	58.3
Total	60	100.0

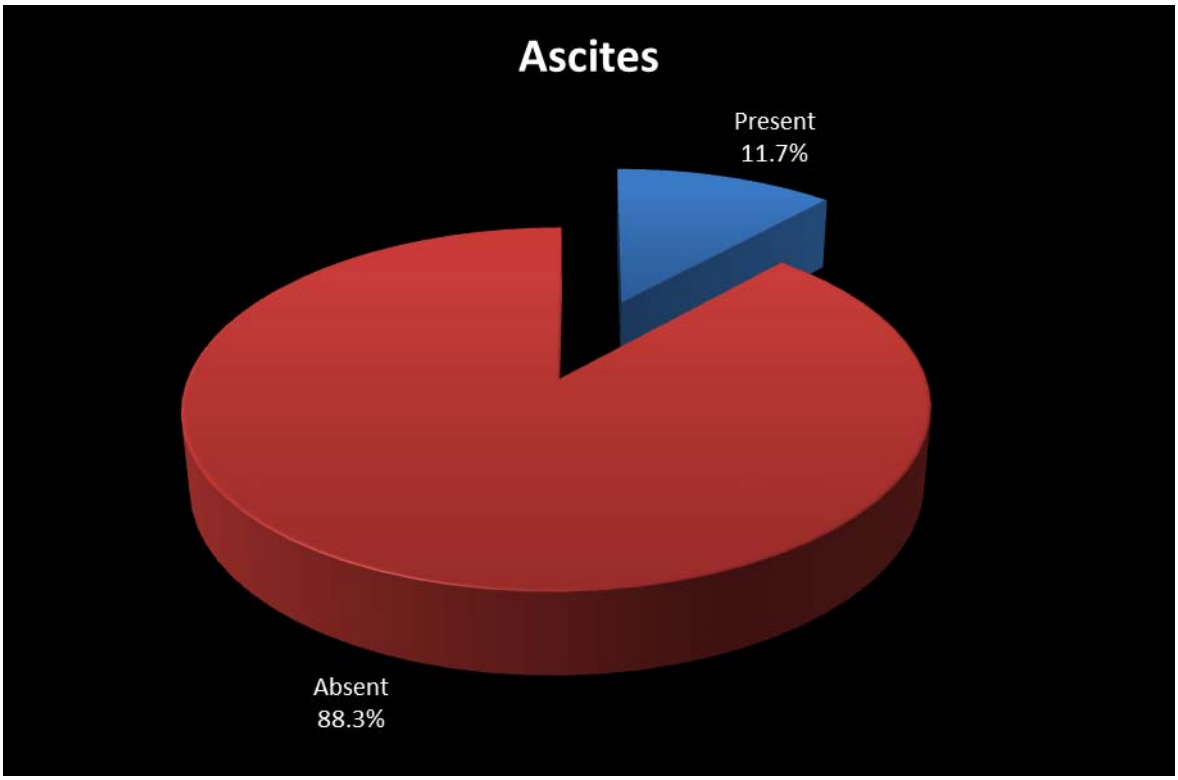


Out of 60 cases studied clinically hepatomegaly was found in 25 cases which forms 41.7% which is in accordance with the observations of Sinha et al and Richman et al[11].

TABLE 8

PRESENCE OF ASCITES IN THE CASES

Presence of Ascites	Frequency	Percent
Present	7	11.7
Absent	53	88.3
Total	60	100.0

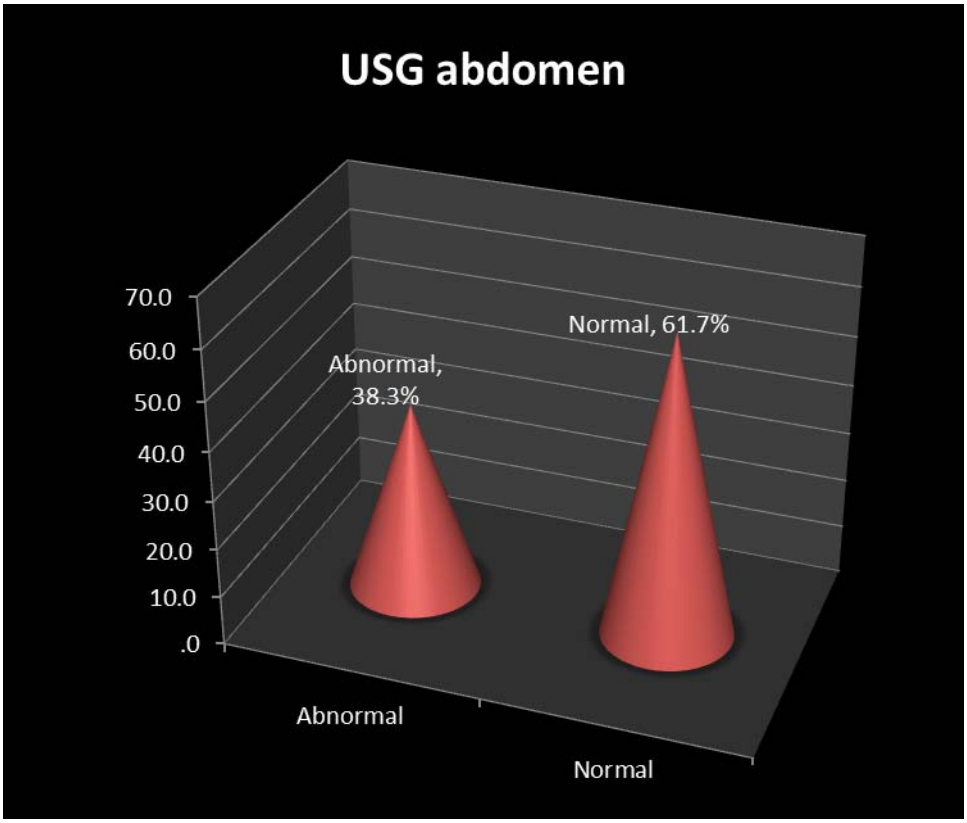


Ascites was clinically made out in 11.7% of cases studied which correlates with findings of Norman et al[12].

TABLE 9

ULTRASOUND ABDOMEN SHOWING CONGESTIVE HEPATOMEGALY IN THE CASES

USG Abdomen with congestive liver	Frequency	Percent
Present	23	38.3
Absent	37	61.7
Total	60	100.0



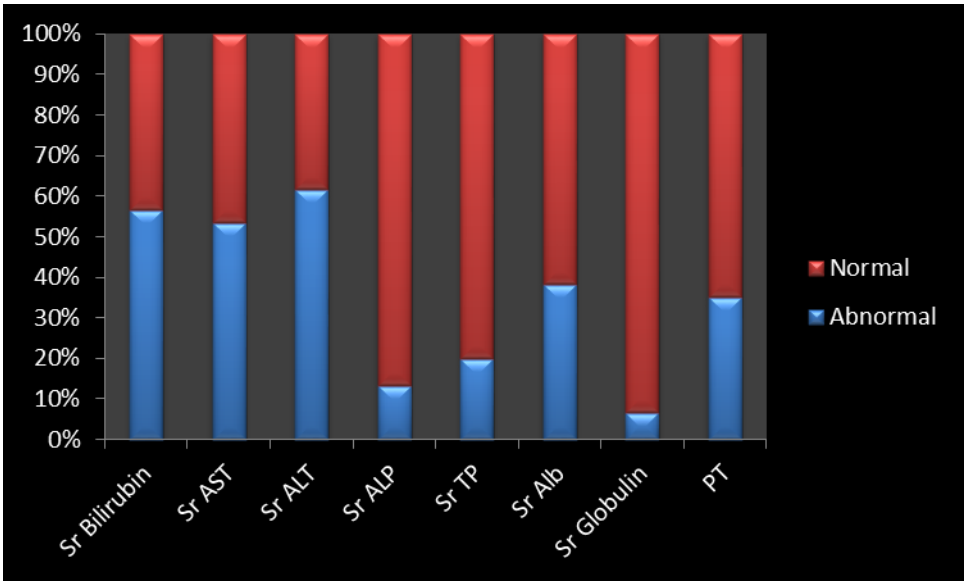
Ultrasound scanning of the abdomen was done in all the 60 cases to identify congestive liver.Of these 23 cases showed abnormality in USG Abdomen(38.3%).

TABLE 10

LIVER BIOCHEMICAL ABNORMALITIES NOTED IN THE STUDY GROUP

Serum Bilirubin	Frequency	Percent
Abnormal	34	56.7
Normal	26	43.3
Total	60	100.0

LIVER PARAMETERS	Abnormal		Normal	
	FREQUENCY	PERCENT	FREQUENCY	PERCENT
Serum Bilirubin	34	56.7	26	43.3
Serum AST	32	53.3	28	46.7
Serum ALT	37	61.7	23	38.3
Serum ALP	8	13.3	52	86.7
Serum Total Protein	12	20.0	48	80.0
Serum Albumin	23	38.3	37	61.7
Serum Globulin	4	6.7	56	93.3
Prothrombin Time	21	35.0	39	65.0



Serum Bilirubin were found to be abnormal in 56.7% of the total congestive cardiac failure patients included in this study.Serum AST was found to be abnormal in 53.3% of the subjects and serum ALT was abnormal in 61.7% of the cases whereas serum ALP was found to be abnormal only in 13.3% of cases thus suggesting a hepatocellular pattern of liver enzyme elevation. Serum albumin was found to be decreased in 38.3 % of the subjects and serum globulin was abnormal in 6.7% of cases. Prolongation of prothrombin time was observed in 35% of cases.

TABLE 11

PREVALENCE OF LIVER FUNCTION ABNORMALITY IN THE STUDY GROUP

LIVER FUNCTION TESTS	Frequency	Percentage
Abnormal	34	56.7
Normal	26	43.3
Total	60	100.0

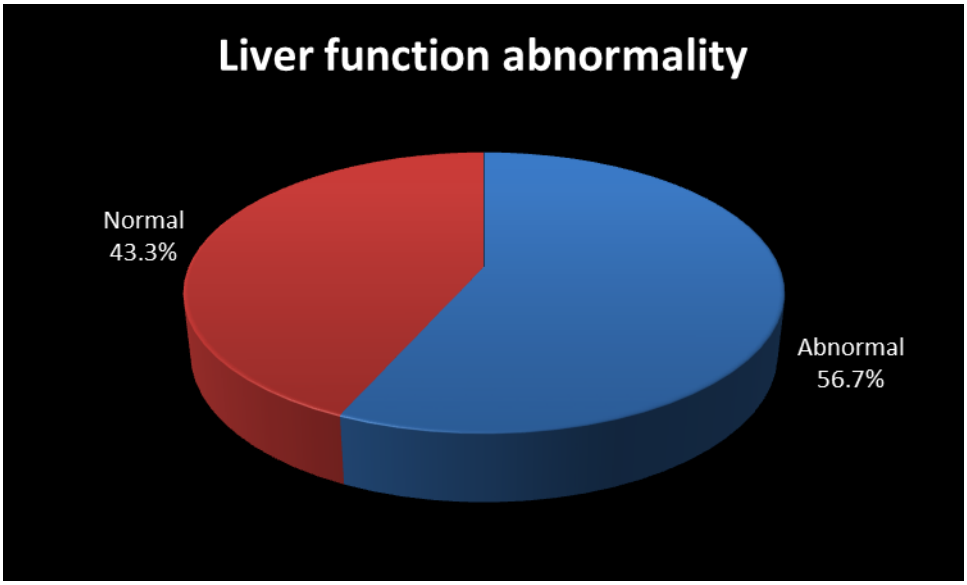


TABLE 12

SHOWING COMPARISON OF MEAN BILIRUBIN VALUES WITH NYHA CLASS OF CARDIAC FAILURE

NYHA CLASS	FREQUENCY	Mean BILIRUBIN	S D	F	p value
Class I	17	1.1	.2	58.555	<0.001
ClassII	22	1.5	.4		
Class III	12	2.3	.5		
Class IV	9	2.9	.5		
Total	60	1.7	.8		

P value less than 0.001 is significant thus suggesting a progressive increase in mean serum bilirubin values with worsening of heart failure class. Class 4 patients showed marked liver function abnormality.

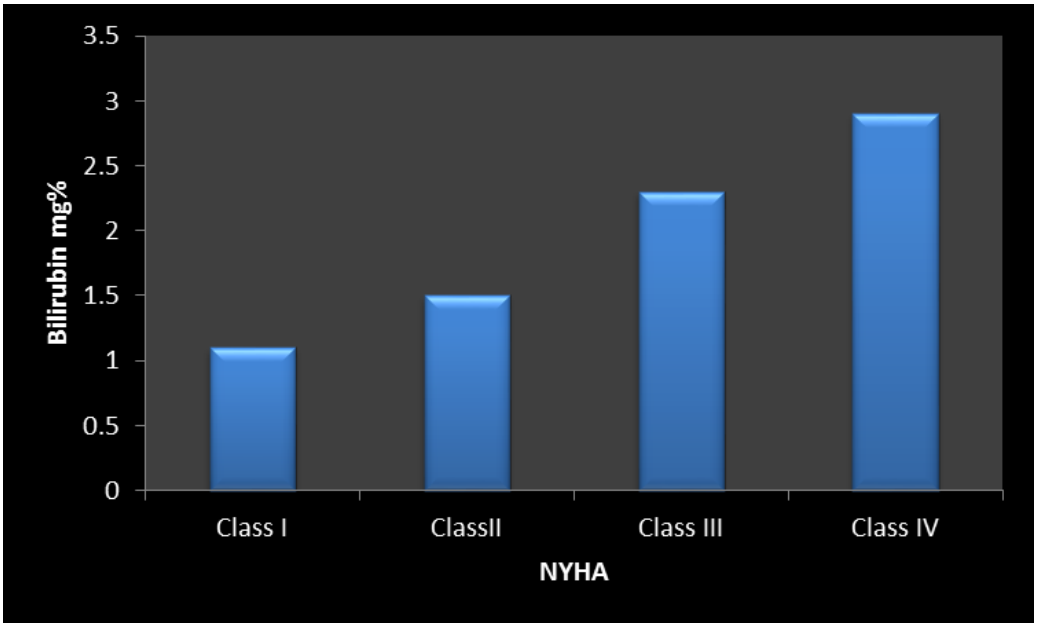


TABLE 13

SHOWING COMPARISON OF MEAN AST VALUES WITH NYHA CLASS OF HEART FAILURE

NYHA CLASS	FREQUENCY	Mean AST VALUES	S D	F	p value
Class I	17	36.9	3.5		
ClassII	22	39.9	5.4		
Class III	12	87.5	41.7	5.171	0.003
Class IV	9	188.8	271.8		
Total	60	70.9	115.0		

This table shows a sequential rise in serum AST levels with advancement of cardiac failure. p value is 0.003 which is significant .

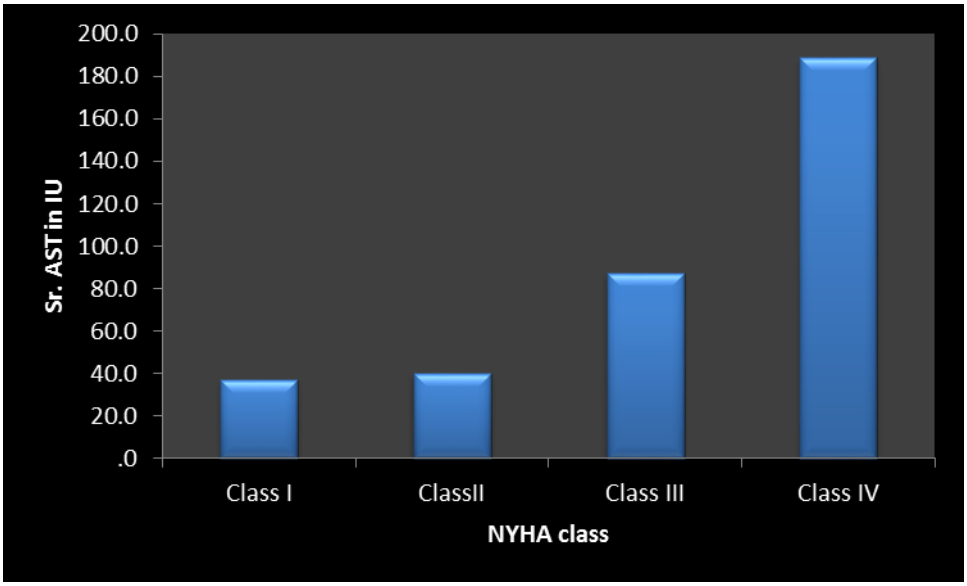


TABLE 14

SHOWING COMPARISON OF DIFFERENT LIVER PARAMETERS WITH NYHA CLASS OF HEART FAILURE

Liver function tests	Nyha class	Frequency in each class	Mean values	S D	F	p value
Serum ALT	Class I	17	32.4	4.0	5.933	.001
	ClassII	22	34.9	6.0		
	Class III	12	81.0	34.5		
	Class IV	9	142.0	186.2		
	Total	60	59.5	80.7		
Serum ALP	Class I	16	44.3	10.8	.336	.799
	ClassII	22	39.5	15.2		
	Class III	12	42.0	18.6		
	Class IV	9	39.4	20.2		
	Total	59	41.3	15.5		
Serum Total Protein	Class I	17	6.4	.2	20.476	.000
	ClassII	22	6.3	.3		
	Class III	12	5.9	.2		
	Class IV	9	5.6	.4		
	Total	60	6.2	.4		
Serum Albumin	Class I	17	3.5	.1	16.646	.000
	ClassII	22	3.4	.2		
	Class III	12	3.1	.2		
	Class IV	9	2.9	.3		
	Total	60	3.3	.3		
Prothrombin Time	Class I	17	13.8	.9	15.706	.000
	ClassII	22	14.3	2.9		
	Class III	12	18.3	3.6		
	Class IV	9	20.2	3.5		
	Total	60	15.8	3.7		

Serum ALP did not show a progressive rise in mean levels with advancing heart failure.p value is.799 which is not significant. All other liver function tests showed a significant change in the mean values with worsening in heart failure class. p values were significant.

TABLE 15

COMPARISON OF SERUM BILIRUBIN WITH ETIOLOGY OF CARDIAC FAILURE

Etiology	SERUM BILIRUBIN				Total	
	Abnormal		Normal			
	Frequency	Percent	Frequency	Percent	Frequency	Percent
CAHD	14	60.9	9	39.1	23	100.0
CP	8	57.1	6	42.9	14	100.0
RHD	7	70.0	3	30.0	10	100.0
CM	4	66.7	2	33.3	6	100.0
HHD	1	14.3	6	85.7	7	100.0
Total	34	56.7	26	43.3	60	100.0

χ^2 =6.255 df =4 p=0.181

p value insignificant

Serum bilirubin did not show much correlation with the etiology of cardiac failure.

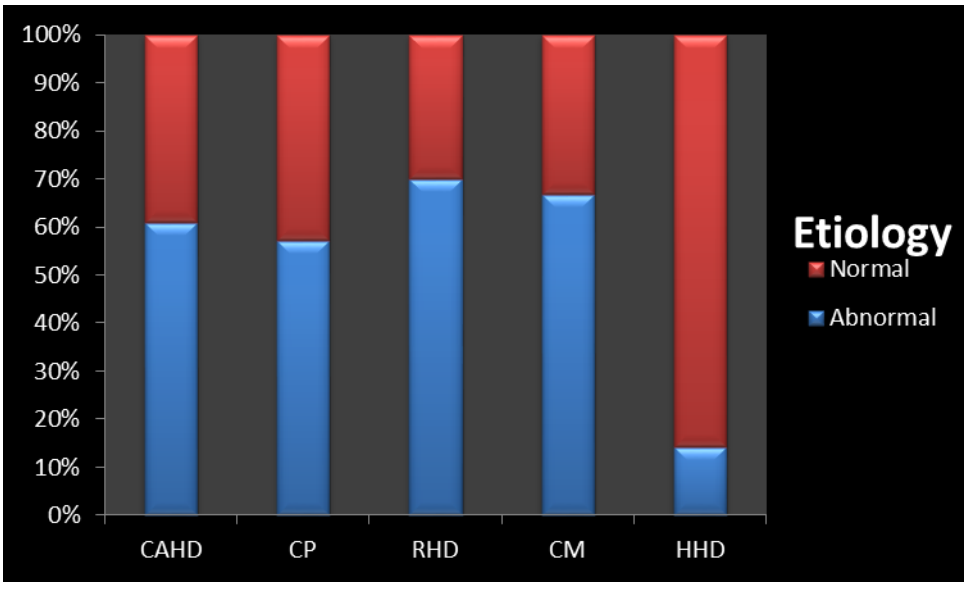


TABLE 16

COMPARISON OF SERUM BILIRUBIN WITH DURATION OF CARDIAC FAILURE

Duration of illness	SERUM BILIRUBIN				Total	
	Abnormal		Normal			
	Frequency	Percent	Frequency	Percent	Frequency	Percent
<1	0	.0	1	100.0	1	100.0
1-5	18	51.4	17	48.6	35	100.0
>5	16	66.7	8	33.3	24	100.0
Total	34	56.7	26	43.3	60	100.0

$\chi^2 = 2.676$ $df = 2$ $p = 0.262$

p value is not significant

No correlation was made out between serum bilirubin and duration of cardiac failure.

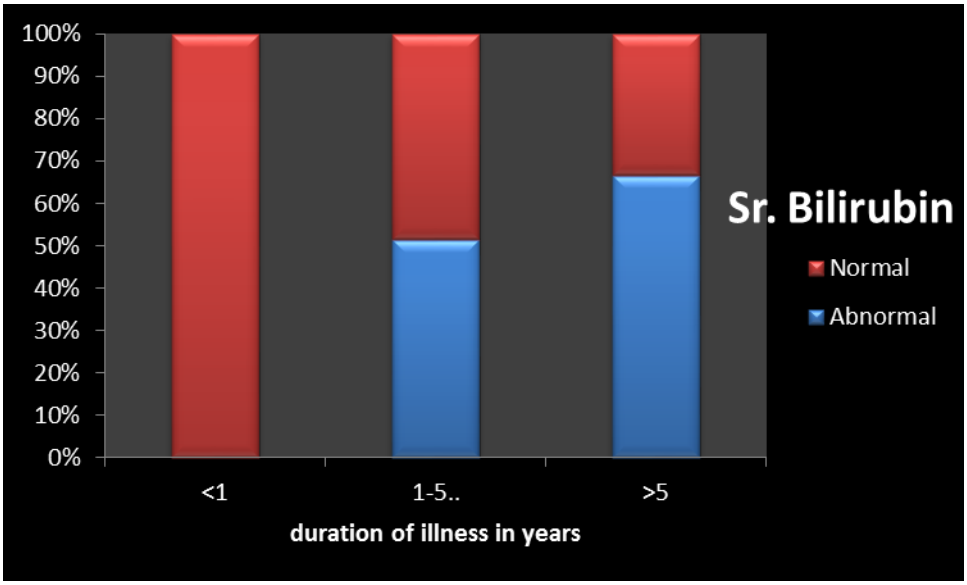


TABLE 17

SHOWING COMPARISON OF MEAN BILIRUBIN WITH OUTCOME OF CARDIAC FAILURE

Outcome	Frequency	Mean Bilirubin	S D	T	P value
Dead	4	2.95	.68	3.603	.001
Alive	56	1.65	.70		

p value is 0.001 which is significant.Elevated serum bilirubin can be considered as a bad prognostic indicator of cardiac failure.

TABLE 18

SHOWING COMPARISON BETWEEN VALUES ON FIRST DAY OF STUDY AND SEVENTH DAY OF STUDY

LIVER FUNCTION TESTS	DAY 1		DAY 7		McNemar test P value
	Frequency	Percent	Frequency	Percent	
Serum Bilirubin	34	56.7	14	25.0	<0.001
Serum AST	32	53.3	16	28.6	0.002
Serum ALT	37	61.7	19	33.9	<0.001
Serum ALP	8	13.3	7	12.5	1.000
Serum TP	12	20.0	8	14.3	1.000
Serum Albumin	23	38.3	27	48.2	0.424
PROTHROMBIN TIME	21	35.0	20	35.7	0.508

p values are significant for Serum Bilirubin,Serum AST and Serum ALT which showed considerable improvement in values with control of failure symptoms and on followup at the end of 1 week. Serum total protein ,serum albumin and prothrombin time did not show significant change at the end of 1 week.

DISCUSSION

Large number of studies has been conducted in evaluating hepatic function in congestive heart failure .Umpteen number of studies are still going on in this arena of liver function.

In this study ,liver biochemical abnormalities and clinical features in cardiac failure because of differing etiologies in 60 patients were recorded ,analysed and compared within and correlated with numerous research papers.The principal intention of this study is to relate indian picture with international scenario.

AGE AND SEX DISTRIBUTION OF THE CASES

Out of 60 patients studied 19 of them belonged to 46- 55 age group and 21 of them belonged to above 55 age group .This shows that cardiac disease and progression into failure is more common in the elderly age group. Out of 60 subjects selected randomly 41 were males and 19 were females which shows the rise in cardiac disease and failure in the male population when compared to the opposite gender which is in correlation with the international scenario. Demographic and Clinical Characteristics of Patients Admitted with Heart Failure in the Euroheart Survey and ADHERE Programmes in the US has shown increased incidence of heart failure in the elderly age group and the male population [1,5]. The median age at first presentation in most recent studies has been in the mid-70s, with a higher incidence in men than in women of all ages. Davies et al in his study

suggest that the occurrence of heart failure is nearly two percent of the adult population, with a sharp increase with age.

ETIOLOGY AND DURATION OF CARDIAC FAILURE

In this study out of the 60 patients studied 23 patients (38.3%) suffered from coronary artery disease, 14 patients from corpulmonale,10 from rheumatic heart disease,6 from cardiomyopathy,7 from hypertensive heart disease.In this study most common cause for heart failure was found to be coronary artery disease which is in correlation with the international scene. The incidence of rheumatic heart disease as the reason for heart failure has declined which is considered as a changing trend in the etiology of heart failure. Cowie et al and Fox et al has shown in there studies the solitary most common cause of heart failure in the developed world is coronary heart disease [1,5,44]. Kannel et al , McMurray et al and levy et al in there studies suggest valvular heart disease and hypertension have come down as the principal reason for heart failure[5].

Out of 60 subjects studied the duration of cardiac failure was greater than 5 years in 24 cases (40%),was in the range of 1- 5 years in 38 cases (58.3) and less than 1year in 1 case(1.7%).

NYHA CLASS

Out of the 60 patients studied 17 belong to class 1,22 belong to class 2,12 belong to class 3,9 belong to class 4. Most of the patients come under

lower clases than higher classes which suggests improved quality of life with cardiac failure medications as reported by Luis et al.

JAUNDICE

Out of the 60 patients studied 20 subjects which is nearly 33% had jaundice. Other causes for jaundice like liver damaging drugs and alcohol related injury were excluded by taking proper history from the subjects. Serological tests were carried out to rule out viral causes for liver damage. Biegus et al has described jaundice clinically 33% of the cases. Similarly Kugel and Lichtman in 1933, Felder et al in 1950, chavez et al in 1943, Sherlock et al in 1951, Evans et al in 1952, Levine and Klatskin in 1964 has suggested in there papers that the serum bilirubin was frequently above the upper limit of normal range.

HEPATOMEGALY

In this study hepatomegaly was found to be present in twenty five out of sixty subjects which is nearly 41.7%. The enlargement in liver ranged from 1cm to 8cm in these subjects. Dunn et al and white et al has demonstrated liver enlargement in more than 90% cases in there studies[24]. Richman et al and Sinha et al found liver enlargement which was above 5cm in nearly fifty percent cases[11].

ASCITES

Out of 60 subjects only seven persons showed clinically detectable ascites which is 11.7%. Norman et al demonstrated ascites and oedema in 15% of cases of cardiac failure studied[12].

ULTRASOUND ABDOMEN

USG Abdomen was carried out in all the 60 subjects. 23 (38.3%) of them showed changes of congestive hepatomegaly in the abdominal scan.

HYPERBILIRUBINAEMIA

Elevated serum bilirubin values were detected in 34 out of 60 patients which is 56.7%.In this study most of them had bilirubin values less than 3mg/dl. Serum bilirubin values were less than 3mg/dl in 55 cases and more than 3mg/dl in 5 cases. Those with values more than 3 showed features of severe congestive cardiac failure. It was seen that with control of cardiac failure the serum bilirubin levels returned to basal values in more than 50% of the cases In this study no specific correlation (p value not significant) was found between etiology and mean serum bilirubin values though subjects with rheumatic heart diseae showed a slight increase in incidence of jaundice followed by coronary heart disease . Hypertensive heart disease patients showed least rise in serum bilirubin values. Similarly no significant correlation was found between duration of cardiac failure and mean serum bilirubin values.

Felder et al has shown elevate bilirubin levels in 52% of the cases in his study [10]. Similarly Wahi et al and Naresh bhu have reported hyperbilirubinaemia in 45% and 58% of subjects respectively. Kubo et al have reported that bilirubin values rarely increase more than 5mg% and are usually less than 3 mg%[26]. Sherlock et al have also reported similar findings with indirect fraction more than direct fraction in his study .Richman et al has reported that control of cardiac failure led to return of serum bilirubin values to basal levels in nearly one week which correlates with the findings in this study[16].

In this study it was noted that as the NYHA Class of heart failure advanced the mean serum bilirubin level also progressively increased which suggests higher classes of heart failure were associated with higher degree of liver dysfunction This was supported by Luiz et al in their study[43].

SERUM AMINOTRANSFERASES.

In the present study 32 subjects (53.3%) showed increased AST levels and 37 subjects (61.7%) showed raised ALT levels. The rise in AST levels ranged from 40-910 IU which correlates with the findings of Richman et al who observed striking rise in transaminase in cardiac failure secondary to cor pulmonale or tricuspid regurgitation or hypotension and shock . Dunn et al and Richman et al have observed that rise in serum ALT is noted in 5-50% of patients and it is seen more in acute heart failure than chronic heart failure. In this study it has been observed that mean AST levels increase

progressively as the NYHA class of cardiac failure progresses. Serum AST levels showed significant elevation in the class IV heart failure which correlates with the observations of the Luiz et al and walter et al. With control of cardiac failure more than 50% values came to the baseline values.

SERUM ALKALINE PHOSPHATASE

In this study out of the 60 subjects studied eight patients showed abnormal serum ALP (13.3%). Felder et al observed elevated serum ALP in ten – twenty percent of subjects studied[10]. Sherlock and Richman has recorded similar observations in their studies[12]. Rise in serum ALP does not relate with the elevation in serum transaminases and bilirubin. ALP values return to basal level with control of failure symptoms. Serum ALP values showed no correlation with the NYHA Classes of cardiac failure. It was observed that mean ALP levels showed no progressive change with worsening of heart failure.

In the present study serum AST and ALT showed marked elevation than serum ALP thus suggesting a predominant hepatocellular pattern of hepatic damage.

SERUM PROTEINS

In this study 23 subjects showed hypoalbuminaemia out of 60 subjects ie 38.3% and 4 cases showed abnormal globulin.AG Reversal was noted in 4 cases. It was noted that with advancement in class of cardiac failure mean

serum albumin levels showed a progressive fall with class IV patients showing the lowest mean serum albumin value with a significant p value. Richman et al in his study has reported decreased albumin in thirty – fifty percent of cases.Mild decrease in albumin levels were observed with values ranging from 2.5g/dl to 2.9g/dl.it was observed by Dunn et al that cases with marked fluid retention showed albumin values less than 1.5g/dl[24]. Serum albumin values usually return to normal in a period of few months following control of cardiac failure.

Elevated globulin values were noted in 35-50% of subjects with right heart failure by Richman et al. A mild rise was noted in most of the cases ranging from 3.5 -4.1g/dl. A rise in globulins and fall in albumin causes reversal of Albumin globulin ratio.It was found that unlike other parameters globulin values did not return to normal value following control of cardiac failure.

PROTHROMBIN TIME

In this study 21 out of 60 patients showed prolongation in prothrombin time(35%).most of the values were 1.5 – 2 times the normal value.Following treatment prothrombin time repeated at the end of 1 week did not show any improvement. Mean prothrombin time also showed progressive increase with worsening of cardiac failure such that class IV cases showed highest mean prothrombin time. White et al as described prolonged prothrombin time in

nearly 85% of the subjects.it was reprted that prothrombin time come to baseline values usually two – three weeks after control of cardiac failure.

OUTCOME

Out of 60 cases studied 4 cases succumbed to the cardiac illness during the course of illness .The mean bilirubin value of these cases were 2.95 which was more when compared to other subjects which was 1.65 with a p value of .001 which is significant suggesting that elevated bilirubin levels can be taken as a bad prognostic marker in congestive cardiac failure.

CONCLUSIONS

1. The most common cause of congestive cardiac failure in patients presenting to Tirunelveli Govt Medical College Hospital was found to be Coronary artery disease.
2. Elderly Male population were found to have an increased incidence of cardiac failure when compared to the opposite gender.
3. Liver function abnormalities were found in 56.7% of the total congestive cardiac failure patients included in this study.
4. Liver function abnormalities did not show any correlation with the aetiology and duration of cardiac failure though subjects with rheumatic heart disease showed a mild increase in incidence of abnormal liver function. Least incidence of liver function abnormalities were found in Hypertensive heart disease patients.
5. Serum AST was found to be abnormal in 53.3% of the subjects and serum ALT was abnormal in 61.7% of the cases whereas serum ALP was found to be abnormal only in 13.3% of cases.This suggest a predominant hepatocellular pattern of liver injury than cholestatic pattern.
6. Serum albumin was found to be decreased in 38.3 % of the subjects and serum globulin was abnormal in 6.7% of cases and A G reversal was noted in 4 cases.Prolongation of prothrombin time was observed in 35% of cases .

7. Mean serum Bilirubin , AST and ALT values when compared with NYHA Class of heart failure showed a progressive increase with the advancement of heart failure . Mean serum ALP values did not show any correlation with NYHA Class of heart failure. Mean serum albumin values showed a progressive fall with advancement of cardiac failure.Prothrombin time also showed progressive prolongation with worsening of failure class. Thus Class IV heart failure patients showed a higher degree of predominant hepatocellular pattern of liver damage.
8. With control of failure and on follow up after one week serum bilirubin and serum enzymes showed considerable improvement whereas serum albumin and prothrombin time did not show any significant change.
9. Out of the 60 subjects studied 4 cases succumbed to the cardiac illness and rest of them showed improvement at the end of 1 week. On comparison of mean bilirubin value with the outcome it was observed that higher values were associated with a poor prognosis. Thus serum bilirubin was found to have prognostic significance in cardiac failure.

BIBLIOGRAPHY

1) Harrison's Principles of Internal Medicine 18TH Edition.
2) Sheila Sherlock ,Diseases of liver and biliary system-11th Edition
3) Sleisenger and Fordtrans Gastrointestinal and Liver Disease 8th Edition
4) Braunwalds heart disease 8th Edition
5) Hursts textbook of The Heart 12th Edition
6) Eric J Topol TextBook of Cardiovascular medicine 3rd Edition
7) Robbins Pathological basis of disease structure and function of liver architecture.
8) Oxford textbook of clinical pathology 2nd Edition
9) Schiffs disease of liver 9th Edition
10) L Felder A Mund Liver functions in congestive heart failure,Circulation vol,9:11 286;1950
11) Mathur and Sinha congestive hepatomegaly 1960
12) N Jollifee Liver in heart failure J.clinical inv 8:419,1930
13) F B Mallory Chronic congestion of Liver J med residents 24:455,1911
14) A Cantarow Liver function studies in congestive heart failureArch Int Medicine 56:521 1935
15) H M Zimmerman and Hillsman Experimental study in chronic congestion of liver Arch path 9:1154,1930
16) H L Jaffee serum phosphatase after bile duct lig in dog Proc soc Exper Biol and Med 31:1179,1934
17) C S Keefer pulmonary infarction and jaundice in MI A Clinical study J Clin Inv 2:375 1926
18) A r Rich and Resnik Mech of jaundice in pulm infarction in heart failure patient

19) R A L ambert Liver pathology in chronic congestion N Y Path society 16:33,1916
20) E Libman jaundice in MI j.a.m.i.a80:1923
21) C Garvin cardiac cirrhosis Am J M Sc 205;515 1943
22) F Scaffner P A Safran EM Study of cell and fibrosis chronic passive congestion of liver in man Am J Path 104 160-5 1981
23) GM Hutchins G W Moore A study of 100 subjects at autopsy Hepatic Morphology in cardiac dysfunction1967;50,447-463
24) G D Dunn K J Breen et al A review of liver in congestive heart failure Am J MedScience 1973,265 174-189
25) R M Ross Hepatic damage secondary to heart failure Am J of GE 1981;76;511-518
26) B A Walter S H Kubo et al Influence of systemic hemodynamics Arch of Int Med 1987,147,1227-9
27) A J Delmann S M Richman Liver function indices alteration in heart failure in ref to enzymes Am J Med 1961 ; 30 211-225
28) L Mendez Morphology of hepatic injury in heart diease and shock J of Hepat 1986 ,2;15-27
29) Keirman et al liver morphology Trans royal soc of London 711 ,1983
30) ET Mesquita Heart failure in Brazil.ion of The EPICA-Niteroi study. Rev Port Cardiol. 2004;23(3):25-30.
31) H C Tan ,GT Lau. Liver dysfunction type in cardiac failure and its association with the severity of tricuspid insufficiency. Am J Cardiol. 2002;90:1405-9.
32) VC Cogger, R Fraser et al . Heart failure and Liver dysfunction. Am J Cardiol.2003;91:1399.
33) Naschitz JE, Lewis RJ, Yeshurun D. Liver diseases affecting the heart and heart diseases affecting the liver and. Am Heart J. 2000;1:140.

34) Ridruejo E, Cingolani O. Atypical form of cardiac failure presentation Fulminant hepatic failure. Medicina (B. Aires). 2000;4(60):491-4.

35) RW Bailey, KC Fuh , S R Hamilton . Ischemic hepatic injury with hemodynamic pathogenesis in shock. Shock. 2000;4(14):451 9.

36) F Pileggi, F Vilas-Boas ,L Kopel . In patients with congestive heart failure acute liver failure due to cardiogenic shock. Arq Bras Cardiol. 1994;427-30.

37) Guallar-Castillon P, Rodriguez-Artalejo F Heart failure and Epidemiology . Rev Esp Cardiol. 2004:161-2.

38) CZ Torres , RA Cox . Adults and acute heart failure. P R Health Sci J. 2004:265-71.

39) LH Lund . Women and heart failure. Med Clin North Am. 2004:1321-45..

40) M Tendera . Heart failure and the epidemiology . J Renin Angiotensin Aldosterone Syst. 2004: S2-6..

41) J .W. McNee, Quart. J. Med., 1922, 16, 390. A Review of jaundice .

42) A M Fishberg J. Am. Med. Assoc., 1923, 1999, 1516. Jaundice in Myocardial Insufficiency.

43) C H Andrews . Quart. J. Med., 1924, 17, 19. Van den Bergh's Test in Jaundice a Clinical Study.

44) Leon, Schiff, Arch. Int. Med., 1927, 800. Serum Bilirubin in Disease and Health.

45) J J Meakins . Clin. Invest., 1927,135. Circulatory Failure and Distribution of Jaundice .

46) I H Page, Am. J. Med. Sci., 1929, 273. Edema and Jaundice Associated with Hemiplegia and Cardiac Decompensation

47) G B Wallace and J S Diamond, Arch. Int. Med., 1925, 698. Urobilogen in the Urine its Significance as a Test for hepatic Function.

48) G M Piersol and M M Rothman J. Am. Med. Assoc., 1928, 1768. Liver Function Tests and its Practical Value .

49) A M Serby and Leon Am. J. Med. Sci.. 1928,367. Liver Function in Seventy-Six Cases as Determined by Bromsulphalein .

50) Epstein, N. N, and Kerr, W. J. J. Am. Med. Assoc., 1927, 1619. The Rose Bengal Test in hepatic function.

51) R Ottenberg , L Goldsmith . Arch. Int. Med., 1924, 206. The Serum Tetrachlorphenolphthalein Test for Liver Function and its Clinical Value

52) K. H Tallerman. Quart. J. Med., 1923, 37. An Investigation of the Hepatic Condition in Pregnancy The Levulose Test for Liver Efficiency .

53) Hall W. W, J. Lab. and Clin. Med, 1927, 529. Notes on Interpretation and Technic of the van den Bergh Reaction for Serum Bilirubin .

54) S M Rosenthal and E C White J. Am. Med. Assoc. 1925, 1112. Bromsulphalein Test for Hepatic Function A Clinical Application .

55) W W Greenway.CV Conceptual review of the hepatic vascular bed.hepatology journal 1987.7.952-963.

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PROFORMA

Name

Age

Sex

I P NO:

PRESENTING COMPLAINTS

DURATION

Chest pain :

Breathlessness :

Palpitations :

Syncope :

Cough :

Haemoptysis :

Swelling of legs :

Oliguria :

Fever :

Other symptoms :

PAST HISTORY

Similar illness in the past

Diabetes mellitus

Hypertension

Coronary artery heart disease

Bronchial asthma

Jaundice

Rheumatic fever

Pulmonary tuberculosis

Transient ischaemic attacks

Abortion / Exposure to sexually transmitted diseases

PERSONAL HISTORY

Smoking

Alcoholism

FAMILY HISTORY

Hypertension

Diabetes mellitus

Coronary artery heart disease

CLINICAL EXAMINATION

Consciousness

Orientation

Temperature

Anaemia

Jaundice

Cyanosis

Clubbing

Pedal edema

Lymph node enlargement

Jugular venous pressure

Signs of infective endocarditis

Signs of liver failure

VITAL PARAMETERS

Pulse

Blood pressure

Respiratory rate

CARDIOVASCULAR SYSTEM

Heart sounds and murmurs

Parasternal heave

Abnormal pulsations

RESPIRATORY SYSTEM

Respiratory rate

Breath sounds

Added sounds

ABDOMEN

Appearance

Ascites

Hepatomegaly

Spleenomegaly

CENTRAL NERVOUS SYSTEM

Higher functions

Cranial nerves

Spinomotor system

Sensory system

Cerebellar system

Spine and cranium

DIAGNOSIS

Onset of illness Acute

Chronic

Acute on chronic

Duration of illness < 1 Year

1-5 Years

> 5 Years

INVESTIGATIONS

Blood hemogram

Urine routine

Blood sugar

Blood urea and serum creatinine

Serum electrolytes

HBs Ag

Anti HCV Abs

Electrocardiography

Chest x ray

13. LIVER FUNCTION TESTS

S.Bilirubin- Total

Direct

Indirect

SGOT

SGPT

Alkaline Phosphatase

Total Proteins

Albumin

Globulin

AG ratio

Prothrombin time

14. USG abdomen

MASTER CHART

SL NO	NAME	AGE	SEX	ETIOLOGY	DURATION			J	H	A	Class of CCF	S.BIL		AST		ALT		SAP		S.PROTEINS						PRO.T				USG ABD
					1	`5	~5					D1	D7	D1	D7	D1	D7	D1	D7	D 1			D 7			D1		D7		
																				T	A	G	T	A	G	C	T	C	T	
1	SELVARAJ	45	M	CAHD		*		-	+	-	4	3.6	1.5	910	180	636	98	41	40	6	3.2	2.8	6.2	3.2	3	12	24	12	22	+
2	KASIPANDI	53	M	CAHD		*		-	-	-	2	1.8	1.2	41	32	36	30	19	28	6.5	3.7	2.8	6	3.2	2.8	14	12	14	14	-
3	MUTHUSAMI	58	M	CP			*	-	-	-	3	1.6	1.2	42	40	35	33	29	29	6	3.2	2.8	6	3	3	14	14	14	16	-
4	LAKSMI	39	F	RHD			*	+	+	+	4	2.6	1.4	59	40	47	38	19	17	5.2	2.7	2.5	5.4	2.9	2.5	14	22	14	24	+
5	KUMAR	48	M	CAHD		*		-	+	-	2	1.4	1.2	44	38	38	32	14	14	6.5	3.5	3	6.2	3.2	3	14	12	12	12	+
6	CHINNASAMI	40	M	CM		*		+	+	+	4	2.8	1.8	98	142	68	128	18	14	6.4	3.4	3	6.8	3.6	3.2	14	12	14	14	+
7	VALLI	46	F	HHD			*	-	-	-	1	1.2	1.0	38	32	36	31	21	16	6.2	3.4	2.8	6.4	3.4	3	12	14	12	14	-
8	PANDI	51	M	CAHD	*			-	-	-	2	1.0	0.8	44	38	38	36	18	16	6.2	3.2	3	6	3.2	2.8	14	14	14	14	-
9	MARIAMMAL	48	F	CAHD		*		-	-	-	2	1.8	1.4	48	42	44	38	14	12	6.4	3.4	3	6	3	3	14	16	14	14	-
10	GANESAN	58	M	CP			*	-	+	-	3	2.4	1.4	40	38	38	36	12	10	5.8	3.	2.8	6.0	3.2	2.8	14	16	14	16	+
11	RAMU	44	M	RHD			*	-	+	-	3	2.8	1.4	182	48	148	34	39	35	5.6	3.2	2.4	6.0	3.4	2.6	14	14	14	14	+
12	KANNAN	51	M	CAHD		*		-	-	-	2	1.2	.8	29	26	26	24	38	34	6.5	3.5	3	6.5	3.5	3	14	14	14	12	-
13	GOMATHI	56	F	CM		*			+		3	2.8	1.4	148	48	126	36	30	30	5.6	2.6	3	6.4	3.0	3.4	14	22	14	22	-
14	SAMUEL	59	M	CP		*			+		4	3.2	2	88	36	78	32	30	28	5.2	3.2	2	5.4	3.2	2.2	14	22	14	22	+
15	SAROJA	30	F	HHD		*					1	1.4	.8	41	41	32	29	33	31	6.5	3.5	3	6.6	3.6	3	14	14	14	14	-
16	SHEIK AHAMMED	52	M	CAHD		*			+		4	3.4	1.4	93	42	83	32	38	35	5.4	2.4	3	6	2.8	3.2	14	18	14	16	+
17	DEVI	28	F	RHD			*		+		3	2.8	1.2	84	44	76	32	30	36	5.8	3.	2.8	6	3.2	2.8	14	22	14	20	+
18	POOMANI	49	F	CAHD		*			_		1	1.4	1.2	38	33	34	31	44	43	6.5	3.5	3	6.6	3.6	3	14	14	14	12	-
19	ARJUNAN	62	M	CP			*		-		2	1.8	1.4	32	28	30	26	34	32	6.5	3.5	3	6.5	3.5	3	14	12	14	14	-
20	DURAI	34	M	CM		*		+	+	+	4	3.2	3.2	156	243	97	168	32	38	5.2	2.8	2.4	5.4	3	2.4	14	22	14	24	+
21	MARIYAM	38	F	RHD			*	-	-	-	1	.8	.8	30	32	37	31	34	32	6	3.3	2.7	6	3.5	3	14	13	14	14	-
22	ESTHER	62	F	CAHD		*		+	+	-	4	2	2.2	87	135	75	125	33	39	5.4	2.8	2.6	5.4	2.6	2.8	14	22	14	24	+
23	SELVAM	72	M	CP			*		+	-	2	1.9	.8	42	38	32	32	38	34	6	3.5	2.5	6.2	3.2	3	14	22	14	20	+
24	RAMIAH	48	M	CAHD		*			+	-	2	1.8	1.2	54	38	44	36	38	36	6	3	3	6.2	3.2	3	12	18	12	20	+

25	SUBBIAH	54	M	CAHD		*			+		2	2.2	1.2	42	40	34	30	31	32	6.4	3.4	3	6.5	3.4	3.1	14	14	12	14	+
26	ISMAIL	59	M	CP		*			-		1	.9	.8	38	34	36	30	39	38	6.5	3.5	3	6.4	3.4	3	14	16	14	14	-
27	IBRAHIM	68	M	CAHD			*		+		2	2	2.4	38	52	44	58	31	38	6	3.4	2.6	5.6	3	2.6	14	22	14	24	-
28	AMBIKA	54	F	CAHD		*					1	.8	.8	38	34	34	32	33	34	6.5	3.5	3	6.5	3.5	3	14	12	14	14	-
29	SUGUNAN	42	M	CM		*		-	-	-	1	1.0	.8	42	37	38	32		47	6.2	3.2	3	6.5	3.5	3	14	12	14	14	-
30	MANI	75	M	CAHD			*	-	-	-	2	1	.7	41	39	38	36	48	44	6.2	3.2	3	6.4	3.4	3	14	14	14	16	-
31	KALIAMMAL	37	F	RHD			*	-	-	-	2	1.2	.8	44	42	38	36	34	31	6.4	3.4	3	6.2	3.2	3	14	14	14	12	-
32	PARAMESHWARI	56	F	CAHD		*		+	+	-	3	2.4	1.8	93	43	88	38	43	38	6	3.2	2.8	6	3.2	2.8	14	22	14	20	+
33	GANESHAN	60	M	CP		*			+	+	2	2.2	1.2	38	32	44	42	38	36	5.4	2.6	2.8	5.4	2.8	2.6	14	14	14	14	+
34	CHELLADURAI	58	M	HHD			*	-	-	-	2	1.1	1	36	32	38	34	44	42	6.5	3.5	3	6.5	3.5	3	14	12	14	14	-
35	NAINAR	55	M	CAHD		*		-	-	-	1	1	1	38	34	36	32	44	41	6.4	3.4	3	6.4	3.4	3	14	14	14	16	-
36	KRISHNAN	65	M	CP		*		-	-	-	2	1.2	1	44	36	38	36	48	46	6.4	3.4	3	6.2	3.2	3	14	12	14	14	-
37	REHMAN	29	M	RHD		*		-	-	-	2	1.4	1.2	34	32	28	26	48	34	6.5	3.5	3	6.5	3.6	2.9	14	12	14	14	-
38	KUMARESAN	60	M	CP			*	-	-	-	2	1.2	1	35	32	26	24	48	43	6	3.2	2.8	6	3.2	2.8	14	12	14	14	-
39	REMANI	55	F	CAHD		*		-	-	-	1	1	1	34	34	28	26	46	44	6.5	3.5	3	6.5	3.5	3	14	14	14	16	-
40	BEER MOIDEEN	52	M	CP		*		-	-	-	1	1.2	1	36	32	28	24	48	46	6.8	3.8	3	7	4	3	14	14	14	14	-
41	RASATHI	56	F	CAHD			*	-	+	-	3	2.4	1.4	84	73	98	96	58	55	5.8	2.8	3	5.8	3	2.8	14	14	14	16	+
42	SANKARAN	62	M	CM		*			+		3	2.2	1.2	88	82	86	81	38	34	6.	3.2	2.8	6	3.4	2.6	14	22	14	24	+
43	VELLACHAMY	70	M	CP			*				2	1.4	1.2	38	34	32	30	48	46	6.4	3.4	3	6.2	3.2	3	14	14	14	14	-
44	RAJAM	35	F	RHD			*				1	1.2	1	38	33	28	25	49	45	6.5	3.5	3	6.5	3.5	3	14	14	14	14	-
45	PONNAIAH	58	M	HHD		*					1	1.2	1	39	33	28	26	48	44	6.4	3.4	3	6.4	3.2	3.2	14	14	14	16	-
46	ANNAMALAI	50	M	CAHD		*		-	+	-	1	1.2	1	36	32	28	26	44	42	6	3.4	2.6	6.2	3.6	2.6	14	14	14	16	+
47	MAHESH	27	M	RHD			*	-	+	_	3	1.8	1,2	88	68	94	92	45	43	6	3.4	2.6	6.2	3.6	2.6	14	20	14	16	+
48	SUNDARAM	58	M	CP		*		-	-	-	2	1.2	1	38	35	28	24	48	44	6.3	3.3	3	6.2	3.2	3	14	12	14	14	-
49	SANTHI	56	F	HHD		*					1	1	1	34	32	28	26	56	53	6.4	3.6	2.8	6.4	3.6	2.8	14	14	14	14	-
50	SREENI	63	M	CP			*		+		3	1.6	1.2	68	60	70	66	43	42	6.2	3.2	3	6	3.2	2.8	14	14	14	14	-
51	KARPAGAM	56	F	CAHD		*		-	-	-	1	0.8	0.8	29	24	28	26	47	54	6.5	3.5	3	6.6	3.6	3	14	14	14	14	-
52	VELCHAMI	52	M	CAHD			*	+	+	+	4	3	2.8	120	97	117	88	78	79	5.8	2.8	3	5.8	2.8	3	14	20	14	16	+

53	THAJUDEEN	62	M	CP		*		-	-	-	2	0.9	0.9	38	32	32	28	56	54	6.4	3.4	3	6.2	3.4	2.8	14	14	14	12	-
54	MARISELVI	36	F	RHD			*	-	-	+	3	2.8	1.6	88	43	76	38	88	89	6	3	3	6.2	3.2	3	14	21	14	14	+
55	ARSUNAN	51	M	HHD		*		-	-	-	1	1.1	1	39	32	34	28	55	54	6.5	3.5	3	6.5	3.5	3	14	14	12	14	-
56	NALLASAMY	49	M	CAHD		*		-	-	-	1	1	1	39	32	37	32	67	56	6.6	3.6	3	6.6	3.6	3	14	14	12	14	-
57	NALLA KANNU	36	M	CM		*		-	-	-	2	1.2	1.2	39	37	32	28	78	72	6.5	3.5	3	6.5	3.5	3	14	14	14	14	-
58	DEVANAYAGAM	62	M	CAHD			*	+	+	+	4	2.6	1.2	88	74	77	64	66	55	6	3	3	6	3	3	14	20	14	20	+
59	IBRAHIM	28	M	RHD			*	+	-	_	3	2.1	1.4	45	33	37	31	49	48	6.2	3.2	3	6.3	3.3	3	14	18	14	16	-
60	RAJAM	52	F	HHD			*	-	-	-	2	1	1	38	36	27	21	55	51	6.8	3.8	3	7	4	3	14	14	14	14	-